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REVIEW

Blast-Related Mild Traumatic Brain Injury: A Bayesian Random-Effects Meta-Analysis on the Cognitive Outcomes of Concussion among Military Personnel

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Abstract Throughout their careers, many soldiers experience repeated blasts exposures from improvised explosive devices, which often involve head injury. Consequentially, blast-related mild Traumatic Brain Injury (mTBI) has become prevalent in modern conflicts, often occuring co-morbidly with psychiatric illness (e.g., post-traumatic stress disorder [PTSD]). In turn, a growing body of research has begun to explore the cognitive and psychiatric sequelae of blast-related mTBI. The current meta-analysis aimed to evaluate the chronic effects of blast-related mTBI on cognitive performance. A systematic review identified 9 studies reporting 12 samples meeting eligibility criteria. A Bayesian random-effects meta-analysis was conducted with cognitive construct and PTSD symptoms explored as moderators. The overall posterior mean effect size and Highest Density Interval (HDI) came to d=−0.12 [−0.21, −0.04], with executive function (−0.16 [−0.31, 0.00]), verbal delayed memory (−0.19 [−0.44, 0.06]) and processing speed (−0.11 [−0.26, 0.01]) presenting as the most sensitive cognitive domains to blast-related mTBI. When dividing executive function into diverse sub-constructs (i.e., working memory, inhibition, set-shifting), set-shifting presented the largest effect size (−0.33 [−0.55, −0.05]). PTSD symptoms did not predict cognitive effects sizes, β_{PTSD}=−0.02 [−0.23, 0.20]. The results indicate a subtle, but chronic cognitive impairment following mTBI, especially in set-shifting, a relevant aspect of executive attention. These findings are consistent with past meta-analyses on multiple mTBI and correspond with past neuroimaging research on the cognitive correlates of white matter damage common in mTBI. However, all studies had cross-sectional designs, which resulted in universally low quality ratings and limited the conclusions inferable from this meta-analysis.

Keywords Blast-related · mild Traumatic Brain Injury (mTBI) · Concussion · Cognition · Executive function

Mild Traumatic Brain Injury (mTBI), also referred to as concussion, has become a recent health concern within the United States military (Hayward 2008); however, much of the research on mTBI to date has involved samples from solely athletic settings (Dougan, Horswill, and Geffen 2013). Although sports-related concussion research can inform military practices and policies (Lew, Thomander, Chew, and Bleiberg 2007), combat-related mTBI remains a particularly unique form of injury, with most head injuries among soldiers resulting from Improvised Explosive Devices (IEDs; Gondusky and Reiter 2005; Murray et al. 2005) and the sequential blast, rather than a blunt-force trauma. Blast-related mTBIs differ largely from sports-related concussions in regards to the mechanisms of injury, with past reviewers extensively detailing the damaging effects of blast waves on the brain (Kocsis and Tessler 2009; Leung et al. 2008). Despite support from animal models (Bauman et al. 2009; Koliatsos et al. 2011), researchers have yet to establish an exact blast-related TBI model; however, current evidence suggests that the blast wave results in over-pressurization followed by under-pressurization (Cernak and Noble-Haeusslein, 2010), which disturbs axonal pathways, damages capillaries and forms cavities within the brain tissue (Rosenfeld et al. 2013). Although the primary blast remains particularly relevant in regards to injury mechanisms, many closed-head mTBIs in military settings are confounded by additional, secondary blunt-force

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impacts to the head (i.e., via projectiles, the body being thrown, or contact with a surface following the blast). In turn, some mechanisms of injury may overlap with that of more common civilian concussions. However, the mere exposure to blast largely distinguishes mTBI in soldiers from concussions in athletes, potentially making it a clinically unique injury with an ominous prevalence among deployed and returned soldiers.

Among the physical injuries recorded in the early stages of the Iraq and Afghanistan wars, 16–29 % involved some wound to the head or neck, despite these areas accounting for only 12 % of the body's surface (Owens et al. 2008; Rustemeyer, Kranz, and Bremerich 2007; Xydakis, Fravell, Nasser, and Casler 2005). With consideration for blast-related mTBI, head or neck combat wounds accounted for a higher proportion of injuries among American troops in Iraq and Afghanistan than previous conflicts (e.g., World War II, Vietnam) and explosions now represent the most common mechanism of wartime injury (Owens et al. 2008). IEDs and mines accounted for 88–97 % of injuries among two samples of American troops wounded in Iraq, with roughly half of these injuries involving the neck or head (Gondusky and Reiter 2005; Murray et al. 2005). In turn, and not surprisingly, IEDs were linked to a preponderance of mTBIs among U.S. Marines in Iraq from 2004 to 2008 (MacGregor, Dougherty, and Galarneau 2011).

Although protective armor and helmets have improved overall survival rates from such injuries, they cannot protect against closed-head injuries induced by blast. For example, closed-head TBI characterizes the majority of head injuries treated at the Walter Reed Army Medical Center in Washington, D.C. (Okie 2005). Blast-related TBI and post-traumatic stress disorder (PTSD) have become "signature" injuries of recent military conflicts and "invisible" wounds of war (Hayward 2008; Tanielian and Jaycox 2008). Notably, PTSD appears to be the most common psychiatric co-morbidity of mTBI (Carlson et al. 2011; Chapman and Diaz-Arrastia 2014; French, Iverson, Lange, and Bryant 2011), with reduced psychosocial functioning (Pietrzak, Johnson, Goldstein, Malley, and Southwick 2009), pain (Hoge et al. 2008), poor sleep (Schreiber et al. 2008), and substance misuse (Tanielian and Jaycox 2008) serving as other psychological and behavioral concerns often linked to the full spectrum of TBI among veterans. From 2000 through the first quarter of 2014, the U.S. Department of Defense (2014) has identified over 300,000 TBIs of any mechanism, with the majority (i.e., 82.4 %) qualifying as mild. Among a sample of 2,525 soldiers returning from Iraq, 4.9 % reported loss of consciousness (LOC) and 10.3 % reported an alteration of consciousness (AOC), indicating a total prevalence of mTBI at about 15 % among returned Iraq veterans (Hoge et al. 2008). Among a U.S. Army sample of 3,952 personnel, 587 self-reported a history of mTBI, with 72.2 % of concussed participants reporting blast-related mTBI, implicating blast in the majority of mTBIs among army personnel (Wilk et al. 2010).

The mere prevalence of military mTBI presents a disconcerting context; however, the within-person frequency of blast exposure among veterans appears even more alarming. With a high frequency of IED-related injuries (Gondusky and Reiter 2005; Murray et al. 2005), soldiers can often be exposed to multiple blasts during their deployment (Benzinger et al. 2009). One individual case study recorded 50 significant blast exposures throughout a veteran's 14-year military career in the U.S. Marine Corps Explosive Ordnance Disposal Service (Hayes, Morey, and Tupler 2012). Further, four empirical studies on blast-related mTBI reported means of over 13 self-reported head injuries among their samples (Matthews, Spadoni, Lohr, Strigo, and Simmons 2012; Nelson et al. 2010; Peskind et al. 2011; Petrie et al. 2014). Among another sample evaluated for lifetime TBI, participants reported a mean of 14 lifetime blast exposures, with a median of 2 and a range of 0 to 511 (Fortier et al. 2014) With this high frequency of repeated mTBI and repeated blast exposure, military veterans may stand at an increased risk of Chronic Traumatic Encephalopathy (CTE), a pathology believed to be triggered by past experiences of multiple mTBIs, along with other dementias (McKee et al. 2013).

Omalu et al. (2011) described the first case of CTE among an Iraqi veteran with PTSD, identifying neuropathology consistent with that observed in athletic samples. Blast-related and sports-related mTBI may share common pathogenic variables that ultimately lead to CTE, specifically the head acceleration that leads to structural damage and neurophysiological dysfunction (Goldstein et al. 2012). Aside from CTE alone, repeated mTBI might place veterans at risk for other neurological disorders, including Alzheimer's disease, frontotemporal lobar degeneration, Lewy body disease, and motor neuron disease (Khachaturian and Khachaturian 2014; McKee et al. 2013). In turn, with the linkage between repeated sports-related concussions and neurodegeneration (Gavett, Stern, and McKee 2011; Guskiewicz et al. 2005; Lehman, Hein, Baron, and Gersic 2012; McKee et al. 2009), the long-term outcome of repeated mTBI for veterans may present a similarly disheartening prognosis, emphasizing the necessity for researchers and clinicians to understand the cognitive and neurological sequelae of blast-related head injury.

To understand the sequelae of mTBI, researchers must identify any brain damage resulting from the injury and link this damage to cognitive processes; however, both neurological injury and neuropsychological impairment remain particularly unclear following blast-related mTBI. Standard neuroimaging techniques, including computed tomography and magnetic resonance imaging (MRI), often fail to detect the subtle injuries following a concussive event (Belanger, Vanderploeg, Curtiss, and Warden 2007). Many researchers

have recently applied Diffusion Tensor Imaging (DTI) to investigate neurological injury following both mixed-mechanism mTBI (e.g., motor-vehicle accidents, falls) and sports-related concussion (Shenton et al. 2012) due to its greater sensitivity at detecting macroscopic white matter differences (Mori and Zhang 2006). Notably, regardless of mechanism, mTBI has been linked to diffuse axonal injury in the brain (Shenton et al. 2012), with traumatic axonal injury serving as the most common outcome of mTBI (Hurley, McGowan, Arfanakis, and Taber 2004). These DTI abnormalities occur predominantly in frontal white matter, with more anterior than posterior damage reported in the mTBI literature (Eierud et al. 2014).

Contrary to sports-related and mixed mechanism mTBI (Shenton et al. 2012), relatively few researchers have begun evaluating white matter damage following blast-related mTBI (Bazarian et al. 2013; Jorge et al. 2012; Mac Donald et al. 2011; Matthews et al. 2011; Matthews et al. 2012; Petrie et al. 2014; Sponheim et al. 2011) and only a handful of these researchers have attempted to link specific injuries to neuropsychological functioning (Sponheim et al. 2011; Jorge et al. 2012; Levin et al. 2010; Mac Donald et al. 2013). Aside from structural damage, functional MRI studies have identified decreases in frontal activity as well (Eierud et al. 2014), which matches recent findings of diminished interhemispheric coordination among frontal regions following blast-related mTBI (Sponheim et al. 2011). General mTBI research and some preliminary specific blast-related mTBI research (e.g., Mac Donald et al. 2011; Petrie et al. 2014; Sponheim et al. 2011) support the conjecture of concentrated damage in frontal and anterior regions commonly following mTBI and corresponding with executive-related deficits (e.g., Lipton et al. 2009; Niogi et al. 2008). However, despite this rationalization, past research on the cognitive sequelae of mTBI does not entirely support the conceptualization of mTBI as a frontal-executive injury, as previous meta-analyses have produced highly variable estimates as to the true effect of mTBI on executive functions (Karr, Areshenkoff, and Garcia-Barrera 2014a).

Numerous empirical studies and meta-analyses have explored the cognitive sequelae of sports-related concussions and mixed-mechanism mTBIs in civilian populations (Belanger and Vanderploeg 2005; Belanger, Curtiss, Demery, Lebowitz, and Vanderploeg 2005; Belanger, Spiegel, and Vanderploeg 2010; Binder, Rohling, and Larrabee 1997; Dougan et al. 2013; Frencham, Fox, and Maybery 2005; Pertab, James, and Bigler 2009; Rohling et al. 2011; Schretlen and Shapiro 2003; Zakzanis, Leach, and Kaplan 1999); however, only a growing body of research has explored cognitive outcomes in the specific context of blast-related mTBI (Bogdanova and Verfaellie 2012). The cognitive sequelae of blast-related mTBI has been historically difficult to measure, due not only to the subtle and subjective impairments often associated with mTBI (French et al. 2011), but also the psychiatric co-morbidities (e.g., PTSD) that often occur following warzone trauma (Lew et al. 2008). The symptoms of PTSD overlap with the many cognitive and symptom complaints associated with concussion, adding to the complexity of co-morbid injury among veterans (Dolan et al. 2012; Vasterling and Dikmen 2012).

Aside from its common co-occurence with PTSD, the mere mechanism of a blast injury makes it a unique form of mTBI. A few empirical studies have evaluated differences in the neuropsychological sequelae of mTBI based on the mechanism of injury, but none of these studies identified any differences between the cognitive outcomes of blast and non-blast related mTBIs (Belanger, Kretzmer, Yoash-Gantz, Pickett, and Tupler 2009; Cooper, Chau, Armistead-Jehle, Vanderploeg, and Bowles 2012; Kontos et al. 2013; Lange et al. 2012; Luethcke, Bryan, Morrow, and Isler 2011; Nelson et al. 2010). Two similar studies assessing post-concussive and neurobehavioral symptoms also found no differences based on the mechanism of injury (Belanger et al. 2011; Lippa, Pastorek, Benge, and Thornton 2010).

Based on these findings, a neuropsychologist may question whether the mechanism of injury truly matters in regards to evaluation and expected rates of recovery. However, at a meta-analytic level, sports-related and mixed-mechanism mTBI showed unique effect sizes across quantitative reviews (Karr et al. 2014a), indicating some potential importance of the injury mechanism or setting. Still, this divergence in cognitive sequelae may derive from study-design differences rather than differences attributable to the injury mechanism itself. Nonetheless, sports-related concussion has become increasingly removed from general mTBI, perceived as a different injury construct (McCrory et al 2013). Similarly, the mere uniqueness of blast injury necessitates further investigation into its specific sequelae, which may diverge from that of other injury mechanisms.

Among the existing research on mTBI, participants reporting multiple concussions are likely the most analogous to military samples, where repeated blast exposure appears common throughout deployment (Benzinger et al. 2009; Fortier et al. 2014). However, the research on repeated mTBI remains extremely sparse and limited, due largely to a reliance on cross-sectional designs and self-report (Belanger et al. 2010). Despite relatively modest effect sizes, executive functions are the most affected by multiple mTBI based on group comparisons (d=.24; Belanger et al. 2010) and second most affected based on correlational analyses (d=.54; Belanger and Vanderploeg 2005), which matches the anterior concentration of neurological injury observed in mTBI (Eierud et al. 2014). Among cognitive constructs, executive functions have been repeatedly discussed in the literature on blast-related mTBI. One case study identified frontal pathology and executive dysfunction as the primary clinical consequences of repeated blast-related mTBI (Hayes et al. 2012)

and a recent review article on blast-related mTBI claimed that the "most common impairments are cognitive deficits in the domain of executive functioning (planning, goal setting, cognitive flexibility and behavioral control), complex attention, and learning and memory" (Bogdanova and Verfaellie 2012, p. 7).

For an evidence-based assessment of military mTBI, clinicians require quantitative evidence about the cognitive sequelae of concussive injuries. Therefore, the current review involved a meta-analysis on the neuropsychological sequelae of blast-related mTBI, looking to empirically evaluate the claim that blast-related mTBI involves primarily executive-related deficits following injury (Bogdanova and Verfaellie 2012). Based on recent neurological evidence (Eierud et al. 2014) and past meta-analyses identifying executive deficits following multiple mTBI (Belanger et al. 2010; Belanger and Vanderploeg 2005), we hypothesized that this cognitive domain would show the most pronounced decrements among military and veteran participants in the post-acute phase following blast-related mTBI (i.e., 90 or more days post-injury). Further, considering the potential influence of PTSD on cognitive outcomes (Dolan et al. 2012), we also explored PTSD symptoms as a potential moderator of cognitive outcomes.

Methods

The report of this meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement provided by Moher, Liberati, Tetzlaff, Altman, and the PRISMA Group (2009).

Literature Search

The literature search occurred in November 2013, with inclusion criteria for the meta-analysis established in advance. To be eligible for inclusion in the meta-analysis on post-mTBI cognitive sequelae, the articles needed to (a) include a group with blast-related/combat-related mTBI in the post-acute recovery phase (i.e., mean time since most recent injury greater than 90 days; Binder et al. 1997; Frencham et al. 2005; Rohling et al. 2011), (b) involve a non-injured control group for comparison, (c) report at least one cognitive outcome measure, either clinically validated or experimental, (d) include only military personnel and/or veterans as participants, (e) report enough information to calculate an effect size, (f) be written in the English language. Researchers did not have to report effort testing for inclusion in the meta-analysis; however, if the researchers specified that a group demonstrated low effort, this sample was not included in analysis.

The literature review involved an online search of the PsycInfo, MedLine, CINAHL, and PsycArticles databases, with results limited to English-language publications involving human participants. The electronic search included mechanism-related (i.e., blast-related, combat-related, blast exposure, and blast-induced), injury-related (i.e., TBI, traumatic brain injury, brain injury, head injury, and concussion) and cognition-related (neuropsycholog*, assessment, and cogniti*) search terms. Figure 1 schematically illustrates the literature search and review process. The electronic search yielded 198 results and a manual search of reference lists gathered 10 additional articles for further review. Ultimately, 9 articles met the inclusion criteria for the meta-analysis. Online Resource 1 includes a list of references for the excluded studies, organized based on their reason for exclusion.

Data Extraction

Two independent reviewers followed a common data collection instrument to independently extract information from each study. Both reviewers extracted study characteristics (i.e., year of publication, sample size, operational definition of mTBI) and participant characteristics (i.e., percent male, age, ethnic composition). As well, the reviewers collected injury characteristics, including the definition of concussion used by the researchers, the mean time since most recent mTBI, and the percent reporting loss of consciousness. As PTSD symptoms relate to cognitive performance following head injury (Bryant 2011), PTSD data was extracted in either continuous measurement scales (e.g., Clinician Administered PTSD Scale) or the percent of the sample diagnosed with PTSD.

In regards to cognitive outcomes, test names were extracted and allocated to a specific cognitive construct based on discussion among authors. Based on previous nomenclature applied in mTBI meta-analysis (Karr et al. 2014a), the authors collapsed the tests into the following cognitive constructs: attention, delayed memory, executive functions, fluency, memory, motor, processing speed, and visual-spatial skills. Considering the differential chronic effects of mTBI on different executive functions (Karr, Garcia-Barrera, and Areshenkoff 2014b), this construct was subdivided into three sub-constructs, as per the approach of Miyake et al. (2000): inhibition, set-shifting, and working memory. As well, both memory and delayed memory were subdivided into verbal and visual categories, considering the differential impact of mTBI on different memory tests (Pertab et al. 2009; Zakzanis et al. 1999).

Table A1 (Online Resource 2) lists the cognitive measures included in the current meta-analysis along with the constructs to which they were assigned. For each cognitive test, the reviewers extracted the mean and standard deviation for the mTBI and control groups in order to calculate an effect size for each measure (i.e., *d*; Cohen 1988). Most all cognitive measurements were included with the exception of global measures linked to performances on more specific tasks with

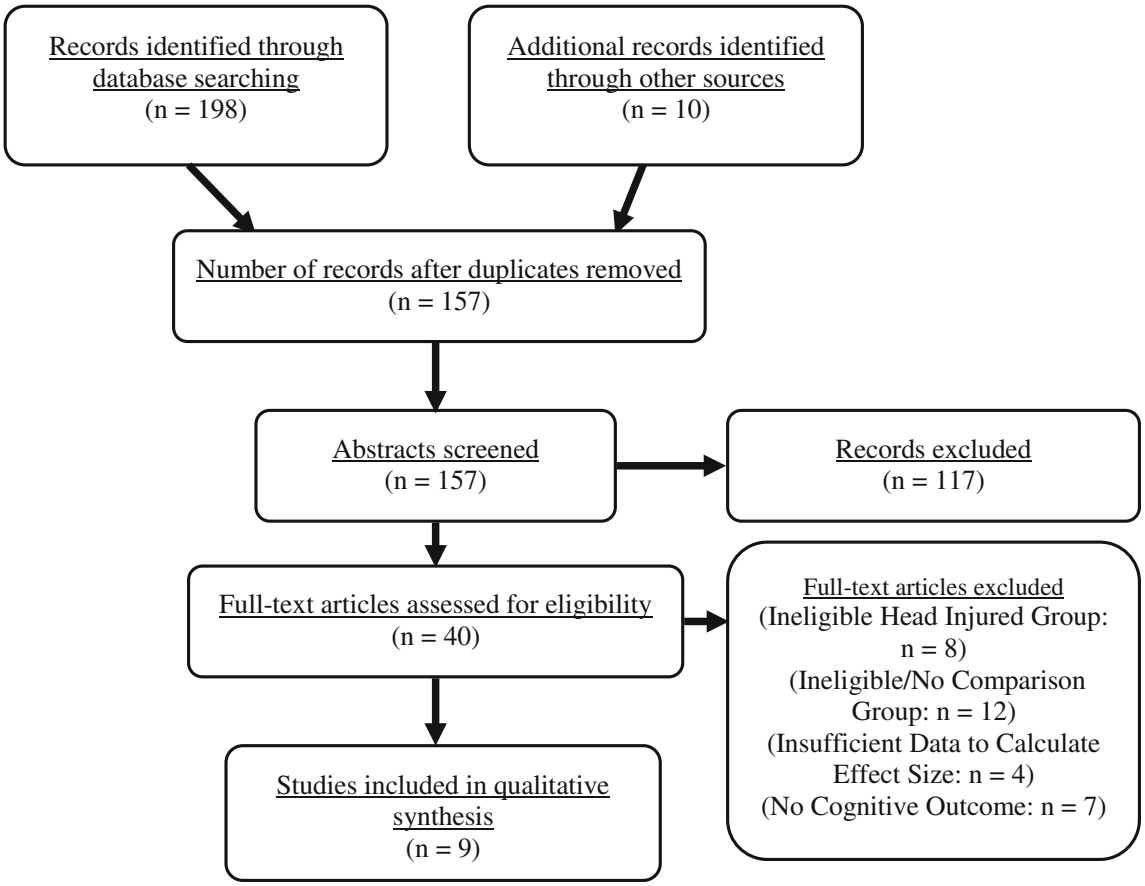

Fig. 1 Flowchart of systematic review

reported data. For example, Nelson et al. (2010) and Vakhtin et al. (2013) both reported overall test battery means, which were not used to calculate effect sizes as they derived from individual test scores reported by the researchers. Similarly, Cooper et al. (2012) reported a total score for the Repeatable Battery for the Assessment of Neuropsychological Status, also not included as an effect size, due to its dependency on more specific subtest scores also reported by these authors. Notably, effort measures, intelligence quotients, verbal comprehension and academic-focused tests (e.g., adult reading) were not extracted as cognitive outcomes (i.e., Vakhtin et al. 2013; Lange et al. 2012; Nelson et al. 2010, 2012; Shandera-Ochsner et al. 2013), as these measures serve to assess malingering or premorbid functioning (Vanderploeg and Schinka 2004).

The majority of studies reported sufficient data for effect size calculation from observed experimental data; however, Vakhtin et al. (2013) and Peskind et al. (2011) did not report means and variances for their control groups, but instead compared standardized scores of their mTBI group performances to the population averages on neuropsychological tasks. In turn, the assumed normative values (i.e., T-score= 50±10 for Vakhtin et al. (2013) and z-score 0±1 for Peskind et al. (2011) were used for effect size calculations in conjunction with the sample sizes of the observed control groups.

In regards to demographic data across studies, Nelson et al. (2010) did not divide gender or ethnicity by group, with the same values used for both the mTBI and control groups (Nelson et al. 2010). Similarly, Kontos et al. (2013) did not provide separate demographic data (i.e., gender, mean age) for blast-related mTBI, blunt-trauma mTBI and non-injured participant groups. For this study, only data for the blast-related mTBI and non-injured control group were extracted for inclusion in the meta-analysis, although the same demographics were used for both groups.

The two reviewers also appraised study quality based on a method previous used for concussion research (Comper, Hutchison, Magrys, Mainwaring, & Richards, 2010), ranking studies based on the Oxford Centre for Evidence-based Medicine guidelines (OCEBM Levels of Evidence Working Group, 2011) and further categorizing studies as either Category A or B based on extracted study data. Studies with three or fewer violations of the following criteria received a Category A designation, whereas studies receiving a Category B designation fulfilled fewer than three of these six criteria:

(1) was the sample described in the study representative of the target population; (2) was there an operational definition of the term ‘concussion’; (3) was the control

group matched on more than two variables (e.g. history of concussion, education level, sport, etc.); (4) were the assessors blinded to subjects' group assignment or neuropsychological test results; (5) were the evaluation tools shown or known to be (i) valid and (ii) reliable; and (6) were there [fewer than three] potentially confounding variables present but not described by the authors. (Comper et al. 2010, p. 1261).

The evaluation of study quality allowed for the identification of any studies with significant methodological issues that could have biased their findings more so than other studies included in the meta-analysis. After independent data extraction and study quality rankings, the data from each reviewer were compared to ensure interrater reliability. The data points for effect size calculation and the study quality rankings were 100 % consistent. In regards to study, participant and injury characteristics, reviewers also arrived at 100 % correspondence after discussing a handful of minor discrepancies.

Statistical Analyses

Effect Size Calculation A Cohen's *d* effect size was calculated for every cognitive outcome extracted from the included studies using the following formula (Cohen 1988):

$$d = \frac{x_1 - x_2}{s}$$

Where

$$s = \sqrt{\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2 - 2}}.$$

Here, s_i^2 and n_i are the variance and sample size of group i, respectively.

Bayesian Meta-Analysis Since each study in our analysis reports multiple effect sizes, we adopted a Bayesian random effects model for the meta-analysis (Sutton and Abrams 2001), in which we assume that individual effect sizes are drawn from study level (normal) effect size distributions. As such, we assume that the means of these study level distributions are drawn from a global (normal) distribution that represents the true effect of blast-related mTBI on cognitive ability.

Specifically, let d_{ij} denote the j'th effect size from study i. We claim that d_{ij} is sampled with error from a normal distribution

$$d_{ij} \sim N\left(\mu_{effect_{ij}},\ \sigma^2_{effect_{ij}}\right)$$

Where $\sigma^2_{effect_{ij}}$ is the variance of d_{ij}, given by

$$\sigma^2_{effect_{ij}} = \left(\frac{n_1 + n_2}{n_1 n_2} + \frac{d_{ij}^2}{2(n_1 + n_2 - 2)}\right)\left(\frac{n_1 + n_2}{n_1 + n_2 - 2}\right),$$

Which results in effect sizes with lower variances (i.e., greater certainty as to their true value) receiving higher weight when estimating the study level effect size. The mean of each individual effect is then sampled from a study level distribution

$$\mu_{effect_{ij}} \sim N\left(\mu_{study_i},\ \sigma^2_{study_i}\right)$$

The means of which are, in turn, drawn from the global distribution representing the true cognitive effect of blast-related mTBI

$$\mu_{study_i} \sim N\left(\mu,\ \tau^2\right).$$

A fully Bayesian treatment of the model requires specifying a prior distribution for the top-level parameters μ and σ^2. We selected a relatively non-informative prior for the mean

$$\mu \sim N(0,\ 1000)$$

Whereas, due to the small sample size, we place a more informative prior on the variance (Gelman 2006):

$$\sigma^2 \sim \text{Cauchy}^+(0,\ 1)$$

Which keeps the variance at a reasonable level, given that there may be too few studies to give a reliable estimate.

All posterior mean effect sizes are reported with a Highest Density Interval (HDI), which contains the highest 95 % of the posterior, indicating a 95 % chance that the true effect size lies within that interval. All Bayesian analyses were conducted using RStan (Stan Development Team. 2014) and remaining analyses were conducted using R (R Development Core Team 2008). The RStan code for both the overall meta-analysis and meta-regression is provided in Online Resource 3.

Moderator Analyses We did not analytically explore age, gender or ethnicity as moderators of post-mTBI cognitive outcomes due to the limited variance in these variables across studies; however, PTSD symptom severity was explored as seven studies included a PTSD rating scale as a measurement within their design and nearly all studies included the Clinician Administered PTSD Scale (Blake et al. 1995) as their outcome (Amick et al. 2013; Nelson et al. 2012; Peskind

et al. 2011; Shandera-Ochsner et al. 2013; Verfaellie et al. 2014), whereas two studies (i.e., Kontos et al. 2013; Scheibel et al. 2012) included the PTSD Checklist (Dobie et al. 2002) as an alternative. The data from these scales allowed for the calculation of effect sizes for PTSD symptoms (i.e., Cohen's *d*), calculated using the formula provided above. Thereafter, a hierarchical meta-regression evaluated PTSD effect size as a predictor of the overall cognitive effect size. Using the notation of the previous section, we model

$$d_{ij} = \alpha + \beta x_i + {}_i + \varepsilon_{ij} + e_{ij}$$

where x_i is the PTSD effect size for the i'th study. Here, ${}_i \sim N(0, \sigma^2)$ is the regression error, $\varepsilon_{ij} \sim N\left(0, \sigma^2_{study_i}\right)$ is the study level error, and $e_{ij} \sim N\left(0, \sigma^2_{effect_{ij}}\right)$ is the effect level error, with variance calculated as in the previous section. The model for this analysis extended from the model in the previous section, maintaining a Bayesian framework and including a Cauchy$^+$ (0, 1) prior on the regression variance and a non-informative prior (0, 1000) on the intercept and β parameters. Cognitive construct was also evaluated as a categorical moderator of effect sizes through the Bayesian framework, using the hierarchical method described above to estimate a construct-specific effect size from a study level distribution and then a construct-specific effect size from the global distribution, using the aforementioned priors.

Publication Bias Assessment Evaluating publication bias has many inherent problems, particularly for an analysis with a small sample size (see Thornton and Lee 2000, for a discussion), as it involves a number of assumptions difficult to verify with existing data. To assess the potential influence of publication bias on the meta-analytical findings, we simulated the effect of unpublished null results by adding additional studies with a zero effect size into the model. Specifically, in addition to the eligible studies, we fit the model with the up to 15 hypothetical studies with effect size of zero and a standard deviation of 0.20, with this value representative of the study level estimates obtained from the meta-analysis. We examined plots depicting the change in the posterior mean effect sizes and respective HDIs with the addition of each study to evaluate the robustness of our findings.

Results

Systematic Review

The 9 eligible studies reported 12 groups with a history of blast-related mTBI and 11 non-injured control groups. Two studies included mTBI groups with and without PTSD/Axis I diagnoses (Nelson et al. 2012; Shandera-Ochsner et al. 2013). For these studies, both mTBI groups were included and compared to separate non-injured control groups that matched the mTBI groups in regards to psychiatric symptoms (i.e., PTSD/Axis I comparison groups with no history of head injury). One study reported two mTBI groups (i.e., with and without LOC), with both groups compared to the same non-injured control group for comparison (Verfaellie, Lafleche, Spiro, and Bousquet 2014). Notably, Nelson et al. (2010) also included two samples with a history of blast-related mTBI, but only one of their mTBI groups was ultimately included in the meta-analysis. The excluded mTBI group was recruited from a forensic setting and – on average – presented significantly worse performances than the non-injured control group on measures of effort. Seven studies reported the exclusion of participants for low effort on symptom validity tests (Amick et al. 2013; Nelson et al. 2010, 2012; Peskind et al. 2011; Shandera-Ochsner et al. 2013; Verfaellie et al. 2014) or non-characteristically low scores based on a test manufacturer's criterion (i.e., two standard deviations below the overall sample mean; Kontos et al. 2013). The two studies not reporting effort measures (i.e., Scheibel et al. 2012; Vakhtin et al. 2013) occurred in a highly research-oriented context, with few clear incentives for low effort on behalf of the participants. To control for the possible impact of low effort on these two studies, a post-hoc analysis excluding these two samples recalculated the overall posterior mean effect size, with results described in the following subsection.

Among the included studies, 1,154 participants reported a history of at least one mTBI, with a mean age of 31.27 years (*SD*=2.63) and a mean educational history of 13.90 years (*SD*=0.53). The mTBI samples were on average predominantly male ($\bar{x}$ = 96.97 %, *SD*=2.47) and white ($\bar{x}$ = 91.90 %, *SD*=7.29). About half of the participants reported an mTBI with LOC ($\bar{x}$ = 49.95 %, *SD*=38.87) with an average time since injury of 3.79 years (*SD*=1.03) across the sample. The control groups included 19,673 participants, the majority of which (*n*=19,390) came from a single study (Kontos et al. 2013). These participants had a mean age of 33.72 years (*SD*=6.68) and were predominantly white ($\bar{x}$ = 85.43 %, *SD*=12.95) and male ($\bar{x}$ = 88.37 %, *SD*=11.41). They presented a mean of 14.18 years of education (*SD*=0.79). Study quality appeared largely homogeneous across studies, with all researchers reporting cross-sectional designs, which resulted in a level of evidence of OCEBM Level 4 for all studies. Following the subcategories specified by Comper et al. (2010), nearly all studies fell into Category A, with the exception of Peskind et al. (2011), which fell into Category B. Table 1 summarizes the extracted data from each individual study, along with their respective overall effect sizes.

Table 1 Studies included in meta-analysis: effect sizes and extracted variables

	Group	n	Mean Age (*SD*)	% Male	% White	Mean Yrs. Education (*SD*)	% w/ PTSD	PTSD ES (*d*)	mTBI Def.	% w/ LOC	x̄ TSI (Yrs.)	Number of BRmTBI (x̄; SD)	Study Quality	Cognition ES (*d*, HDI)
Amick et al. 2013	mTBI	34	29.3 (6.6)	97.1	82.4	13.5 (1.6)	85.3	.95	AMS and/or PTA =15 min. to 24 h. or any LOC	82.4	4.9 (3.4)		Lv. 4, A	−.03 [−.17,.11]
	Con.	38	30 (6.3)	78.9	65.8	13.5 (1.5)	47.4							
Kontos et al. 2013*	mTBI	861	29.5 (6.8)	95.9				.76	GCS = 13–15; Normal imaging				Lv. 4, A	−.05 [−.09, .00]
	Con.	19,390	29.5 (6.8)	95.9										
Nelson et al. 2010**	mTBI	38	34.4 (7.8)	93.3	93.3	14.5 (1.9)	31.6		ACRM	31.6	2.9 (1.2)	14.5 (23.2)	Lv. 4, A	−.19 [−.25, −.12]
	Con.	37	33.9 (9.3)	93.3	93.3	14.1 (2.6)	24.3							
Nelson et al. 2012+#	mTBI	18	37.1 (8.6)	100	100	15.1 (2.1)	0	.37	ACRM	11.1		1.5 (0.6)	Lv. 4, A	−.14 [−.23, −.04]
	Con.	28	32.8 (8.5)	85.7	89.3	14.9 (2.2)	0							
	mTBI	34	29.9 (6.0)	97.1	100	13.9 (1.8)	70.6	.55	ACRM	17.6		1.3 (0.6)		−.05 [−.15, .06]
	Con.	24	34.8 (9.6)	91.7	100	14.3 (2.1)	50							
Peskind et al. 2011	mTBI	12	32 (8.5)	100		13.8 (1.9)	83.3		ACRM		3.5 (1.2)	30 (36)	Lv. 4, B	−.14 [−.39,.10]
	Con.	12	53 (4.6)	58.3		15.5 (2.0)								
Shandera-Ochsner et al. 2013+	mTBI	20	29.7 (8.7)	95	90	13.9 (1.7)	0	.98	ACRM		3.7 (2.5)	1.1 (0.3)	Lv. 4, A	−.09 [−.29, .11]
	Con.	21	34.0 (8.9)	90.5	90.5	14.95 (1.6)	0							
	mTBI	21	30.1 (7.4)	95.2	85.7	13.71 (1.6)	100	.81	ACRM		5.7 (4.1)	1.3 (0.5)		−.18, [−.39, .06]
	Con.	19	32.5 (7.0)	89.5	73.7	13.61 (1.3)	100							
Scheibel et al. 2012	mTBI	15	28.7 (6.0)	100		13.8 (1.5)		.95	DoD	80	2.6 (0.9)		Lv. 4, A	−.15 [−.39, .06]
	Con.	15	30.9 (5.6)	93.3		13.6 (1.4)								
Vakhtin et al. 2013	mTBI	13	34.3 (6.6)	100			0		LOC < 30 min.; PTA < 1 day; normal imaging; mild to moderate PCS	76.9		1.5 (0.8)	Lv. 4, A	−.23 [−.45, −.03]
	Con.	50	29.7 (8.4)	100			0							
Verfaellie et al. 2014++	mTBI	53	30.7 (8.7)	96		13.5 (2.0)		.18	ACRM	0	3.2 (1.9)		Lv. 4, A	−.02 [−.09, .04]
	mTBI	35	29.5 (7.9)	94		13.3 (2.2)		.54	ACRM	100	3.8 (1.9)			−.16 [−.25. −.07]
	Con.	39	29.8 (6.6)	95		13.2 (1.9)								

ACRM American Congress of Rehabilitation Medicine, *AMS* Altered Mental State, *BRmTBI* Blast-Related Mild Traumatic Brain Injury, *Con.* Control, *Def.* Definition, *DoD* Department of Defense, *ES* Effect Size, *GCS* Glasgow Coma Scale, *LOC* Loss of Consciousness, *mTBI* Mild Traumatic Brain Injury, *PCS* Post-Concussion Symptoms, *PTA* Post-Traumatic Amnesia, *PTSD* Post-Traumatic Stress Disorder, *TSI* Time Since Injury

*Kontos et al. (2013) did not separate gender or mean age for the blast-related mTBI group and the control group, with the same values reported for each group

** The PTSD group for Nelson et al. (2010) was combined with other anxiety disorders. As well, these authors did not divide gender or ethnicity by group, with the same values used for both the mTBI and control groups

+ Nelson et al. (2012) and Shandera-Ochsner et al. (2013) included more than one experimental and control group

++ Verfaellie et al. (2014) reported one control group that was included in the effect size calculation for both mTBI groups

The sample from Nelson et al. (2010) is represented within the larger sample of Nelson et al. (2012)

Meta-Analysis

The model was fit using three chains of 10,000 samples, of which 2,000 were burn-in samples. The R statistic was <1.01 for all parameters, suggesting that the model converged successfully, a finding confirmed by visual inspection of the chains. A sensitivity analysis was conducted to assess the effects of the harsh prior on the variance, which demonstrated that the resulting estimates were not sensitive to the precise value of the prior used. Figure A1 (Online Resource 4) provides a visual presentation of these results.

Within the following section, a negative effect size indicates worse performance by the mTBI group when compared to the non-injured control group. The posterior mean effect size came to d=−0.12, *HDI* [−0.21, −0.04]. A post-hoc analysis excluded the two samples without effort assessment (i.e., Scheibel et al. 2012; Vakhtin et al. 2013) and recalculated the posterior mean effect size, identifying a similar result, d=−0.10 [−0.17, −0.02]. To evaluate the impact of publication bias of this overall effect, Figure A2 (Online Resource 5) plots changes in the overall posterior mean effect size and HDI with the addition of 15 null effect sizes, demonstrating that – despite more than doubling the included effect sizes with hypothetical null effects – the overall effect size remained reliably nonzero.

When divided by construct, only one effect size presented compelling evidence of being non-zero: executive functions, d=−0.16 [−0.31, 0.00]. When subdivided into three diverse executive functions (i.e., set-shifting, inhibition, and working memory), set-shifting presented the only effect size estimate with an HDI that did not overlap zero, d=−0.33, [−.55, −.05]. Two other constructs, processing speed and verbal delayed memory, presented an HDI that only slightly overlapped zero, d=−0.11, [−0.26, 0.01] and d=−0.19, [−0.44, 0.06], respectively. Table 2 summarizes the overall effect size and the effect size for each constructs along with their respective HDIs. Figure 2 displays the effects sizes and HDIs for each study schematically through a forest plot. Figure 3 provides a forest plot of the overall effect size and the effect size for each cognitive construct along with their respective HDIs.

Aside from cognitive construct, the only other moderator examined was PTSD symptoms, evaluated through a regression model with PTSD effect size serving as the sole predictor of cognitive effect size. The analysis produced an intercept and HDI of α=−0.08 [−0.22, 0.07], a PTSD beta-weight of β=−0.02 [−0.23, 0.20], and an error term of σ=0.31 [0.26, 0.36]; however, only seven studies reported sufficient data to calculate an effect size for PTSD symptoms, which limited the power of this analysis.

Table 2 Effect sizes by cognitive construct

Construct	k	$\bar{x}$	Lower HDI	Upper HDI
Overall	12	−0.12	−0.21	−0.04
Attention	3	−0.05	−1.70	1.88
Executive Functions	11	**−0.16**	**−0.31**	**0.00**
Inhibition	10	−0.08	−0.32	0.16
Set Shifting	8	**−0.33**	**−0.55**	**−0.05**
Working Memory	7	−0.07	−0.38	0.26
Fluency	8	−0.18	−0.50	0.14
Motor	2	0.13	−1.62	1.24
Processing Speed	10	−0.11	−0.26	0.01
Verbal Delayed Memory	8	−0.19	−0.44	0.06
Verbal Memory	10	−0.17	−0.57	0.21
Visual Delayed Memory	4	0.03	−0.55	0.65
Visual Memory	5	−0.03	−0.57	0.46
Visuospatial Skills	3	−0.43	−1.67	0.66

HDI Highest Density Interval, k Number of studies. Bold indicates an effect size that does not overlap zero

Discussion

The current results present a subtle, but reliably negative impact of mTBI on global cognitive ability in the post-acute phase of recovery, with a clear construct-level effect on the executive function of set-shifting. Although the HDI for their effect sizes slightly overlapped zero, performances on delayed memory and processing speed tasks also appeared slightly worse for those reporting a history of blast-related mTBI. The average time since injury of mTBI was 3.79 years; however, the posterior mean for the estimated global effect size presented strong evidence of being non-zero (i.e., d=−0.12, *HDI* [−0.21, −0.04]), indicating a persistent, but very small cognitive deficit among individuals with blast-related mTBI when compared to non-injured controls. Interestingly, the samples included within the current meta-analysis have a mix of single and repeated blast-related mTBI and/or blast exposures. Many studies listed mean frequencies of blast-related mTBI or blast exposures for their samples slightly above one, but two studies reported an average greater than ten (see Table 1). Peskind et al. (2011) described a mean blast exposure of 30 with a range of 5 to 102 throughout participants' military careers. In turn, the chronic effects of mTBI observed herein may derive from the many participants with repeated mTBI included within the eligible samples, as soldiers commonly experience multiple blast exposures during deployment (Benzinger et al. 2009; Fortier et al. 2014), which could result in multiple blast-related mTBIs. As such, the results of the construct analyses, rather than the overall cognitive effect, closely resemble those of meta-analyses on multiple mTBI.

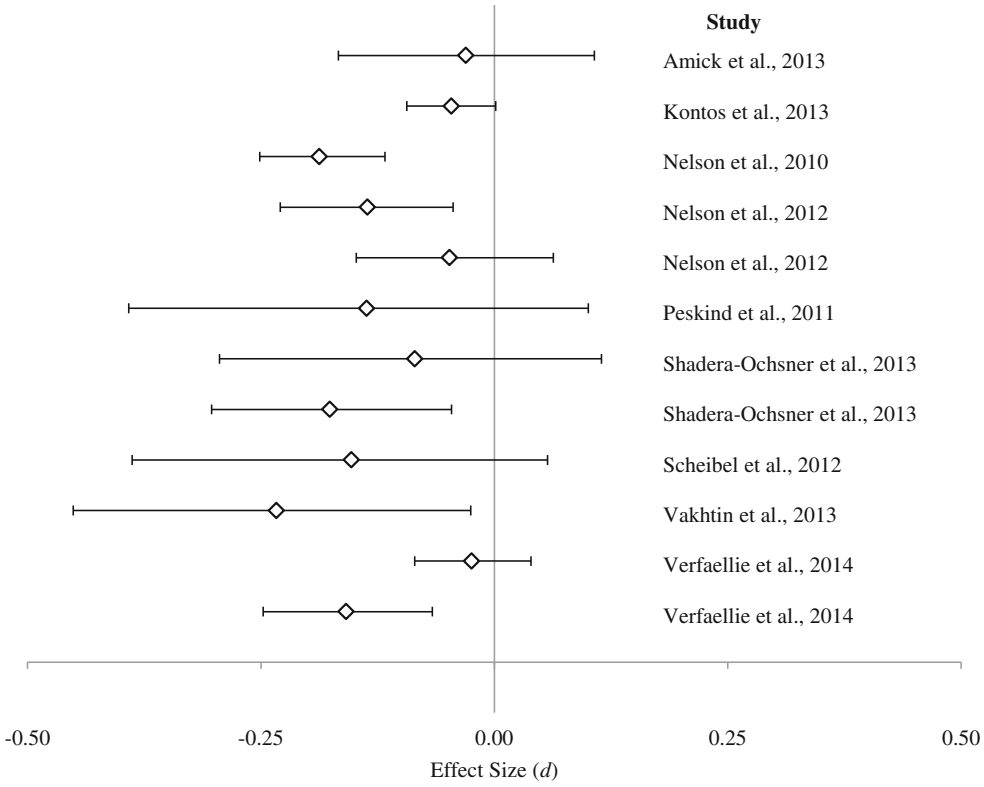

Fig. 2 Forest plot of effect sizes and highest density intervals for each study

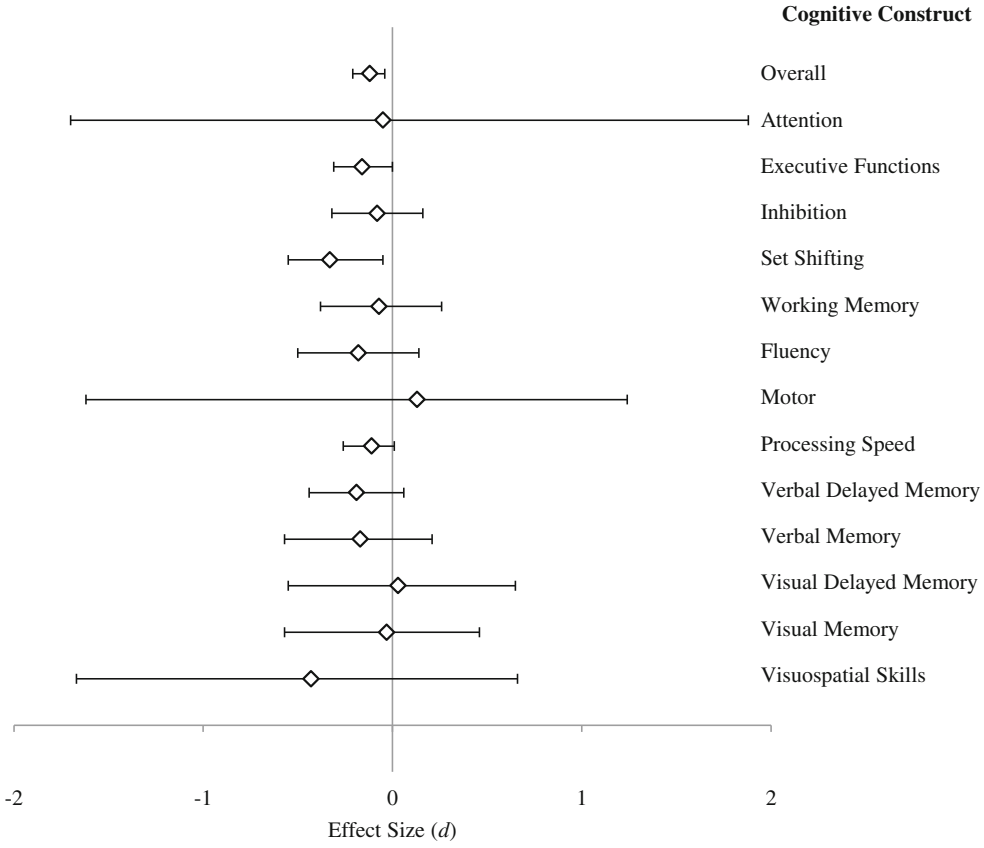

Fig. 3 Forest plot of effect sizes and highest density intervals for each cognitive construct

Interestingly, the construct-level analyses identified executive functions and delayed verbal memory as particularly sensitive to blast-related mTBI, which is consistent with the conclusions of a previous meta-analysis on repeated mTBI (Belanger et al. 2010), despite both meta-analyses including entirely separate groups of studies. Another meta-analysis evaluated exposure to head injury among athletes by evaluating the relationship between cognitive performance and head impact frequencies in sports (e.g., heading the ball in soccer; Belanger and Vanderploeg 2005). These authors similarly identified executive functions and delayed memory as the second and third most adversely impacted cognitive abilities, respectively (language presented the highest effect size). Including the current findings, three discrete meta-analyses evaluating separate populations and exclusive sets of studies all found specific deficits in executive functions and delayed memory following repeated mTBI or an analogous variable (i.e., head injury exposure).

Moving forward from these past meta-analyses, executive functions were investigated as both a unitary and diverse construct in the meta-analysis, which sub-divided executive functions into three constructs: inhibition, set-shifting and working memory (Miyake et al. 2000). Interestingly, set-shifting presented as the only construct with strong evidence for chronic impairment following mTBI, which matches past findings of a post-acute effect of concussion on executive attention tasks in athletes (Halterman et al. 2006; Karr et al. 2014b; Sosnoff, Broglio, Hillman, and Ferrara 2007). Altogether, the construct analyses support the original claim by Bogdanova and Verfaellie (2012), where executive functions, complex attention and delayed memory show impairment following blast-related mTBI. Adding to this conceptualization, the current meta-analysis identified processing speed as an additional construct susceptible to blast-related mTBI.

Brain-Behavior Relationships

Based on the current findings, the cognitive sequelae of mTBI correspond well to the neurological sequelae of mTBI observed in past neuroimaging findings (Eierud et al. 2014). The three constructs presenting evidence of impairment following mTBI (i.e., processing speed, delayed memory and executive functions) have also presented attenuated performances in the presence of white matter abnormalities (Gunning-Dixon and Raz 2000). In terms of white matter damage, traumatic axonal injury stands as the characteristic injury of concussion (Hurley et al. 2004; Shenton et al. 2012) and may even serve as a potential diagnostic feature of the injury (Lee and Huang 2014). In turn, it appears that cognitive impairments following blast-related mTBI match that of common cognitive impairments associated with general white matter damage.

This conclusion corresponds with previous DTI research evaluating associations between axonal damage and cognitive deficits following mTBI, linking post-mTBI global, prefrontal and uncinate white matter damage to processing speed, executive function and memory deficits, respectively (Niogi and Mukherjee 2010). For example, the reduction in attentional control (a construct closely related to set-shifting; Packwood, Hodgetts, and Tremblay 2011) corresponds with localized white matter damage in the anterior corona radiata (Niogi et al. 2008), the most commonly damaged white matter area in cases of mTBI (Eierud et al. 2014). In relation to specifically blast-related mTBI, one study (Jorge et al. 2012) correlated DTI data with executive function and memory measures, finding a correlation between corpus callosum damage and executive performance. Although these authors did not subdivide the corpus callosum in their analysis, they attributed this correlation to anterior components of this commissure, as per past research linking blast-related mTBI to frontal dysfunction and anterior callosal damage (Sponheim et al. 2011). Similarly, a recent DTI study on soldiers with blast and non-blast TBIs of mixed severity (Yeh et al. 2014) found fronto-striatal and fronto-limbic white matter injury, while another study on veterans with blast and non-blast mTBI (Sorg et al. 2014) linked executive performance deficits to damage in the prefrontal white matter, the corpus callosum, and the cingulum bundle (Sorg et al. 2014).

Aside from white matter damage, the cognitive abilities most sensitive to mTBI also match the functional deficits common to the injury, as the frontal processes that underlie delayed memory and set-shifting may also be impaired (Eierud et al. 2014). Past neuroimaging studies have linked verbal information retrieval to predominantly frontal areas, while visual information retrieval relies on more diffuse areas of the brain (Cabeza and Nyberg 2000). As well, set-shifting relies heavily on the anterior cingulate cortex (Posner and Rothbart 2007; Posner, Rothbart, Sheese, and Tang 2007), which has shown functional impairment following mTBI (Mayer, Mannell, Ling, Gasparovic, and Yeo 2011; Witt, Lovejoy, Pearlson, and Stevens 2010). Altogether, the neurobehavioral findings of the current meta-analysis correspond to the neurological findings of past imaging studies, providing quantitative evidence for blast-related mTBI as a largely anterior injury with executive-cognitive sequelae.

Implications for Clinical Practice

Neuropsychologists rely on brain-behavior relationships to appreciate the clinical presentations of brain injury, understanding how lesions in brain areas impact both cognition and behavior. To effectively evaluate head injured soldiers, military neuropsychologists require a comprehensive understanding of both the neurological and cognitive detriments that could be expected after an mTBI in the warzone. With

the current results in mind, a clinician working with military personnel can predict the specific domains (i.e., executive functions, delayed memory, and processing speed) in which long-term deficits may occur following blast-related mTBI. Past clinical recommendations emphasize the assessment of processing speed and memory in the chronic phases of mTBI among those individuals that do not present a timely recovery (Prigatano and Borgaro 2006) and the current findings support the addition of set-shifting as an domain requiring assessment.

In addition to assessment, the U.S. military has established differential treatment algorithms for neuropsychologists evaluating cases of mTBI, with different assessment and treatment plans depending on available resources. One such algorithm (i.e., Initial Management of Concussion in the Deployed Setting; Barth, Isler, Helmick, Wingler, and Jaffee 2010) has the clinician assess symptoms every 3 days and evaluate a differential diagnosis of depression or acute stress if symptoms do not subside by 7 days. To benefit recovery, this algorithm emphasizes psycho-education of the client regarding expected recovery trajectories to facilitate recovery and prompt return-to-duty. With the current findings, neuropsychologists will know which cognitive domains likely remain impaired among soldiers that remain symptomatic in the post-acute phase despite receiving psycho-education, allowing them to identify any cognitive deficits and appropriately structure any supports to ensure safe and timely return-to-duty for injured soldiers.

In addition to acute concussion management, neuropsychologists may have a role at identifying those soldiers chronically impaired by repeated blast-related mTBIs. A history of multiple mTBIs appears as a risk factor for many cognitive concerns among military personnel long after returning home from war, including Alzheimer's disease, CTE, and other neurodegenerative diseases and dementias (Chapman and Diaz-Arrastia 2014; Goldstein et al. 2012; Khachaturian and Khachaturian 2014; McKee et al. 2013). Considering the high cost of dementia care among veterans (Sibener et al., 2014), the early identification of cognitive impairment among brain injured soldiers may eventually serve to predict those at risk for later cognitive declines, although the exact linkage between mTBI and neurodegenerative diseases remains poorly understood to date (Karantzoulis and Randolph 2013). Neuropsychologists have historical roles in the evaluation and management of both brain injuries and dementias, making their understanding of both phenomena invaluable for the care of active-duty and veteran populations.

Limitations and Future Directions

Although the discussed results support a chronic effect of blast-related mTBI, some study design elements (i.e., selection context) and participant characteristics (i.e., PTSD) may have impacted the magnitude of these effects. In regards to selection context, the majority of participants came from health care systems and/or brain injury clinics (e.g., Nelson et al. 2010, 2012; Peskind et al. 2011; Shandera-Ochsner et al. 2013; Scheibel et al. 2012; Vakhtin et al. 2013), which have historically yielded more significant effect sizes among civilian samples (Belanger et al. 2005). In turn, this selection context may inflate the observed effect sizes in the chronic phase of mTBI recovery, due potentially to a selection bias of symptomatic participants that present at such clinics long after injury. Further, those soldiers involved in the medical system may have a unique form of mTBI compared to head-injured soldiers either uninvolved with the medical system or living with an undetected injury.

Aside from selection context, symptom validity remains an ever-present concern in the cognitive assessment of military personnel (Greiffenstein 2010), and minor injuries, such as mTBI, have a higher likelihood of symptom feigning (Greiffenstein and Baker 2008). Nearly all studies reported excluding participants based on evidence of poor effort, but two included studies (i.e., Scheibel et al. 2012; Vakhtin et al. 2013) did not report any assessment of participant effort or symptom validity. Notably, these studies occurred in a research context with no clear incentives for the poor effort or symptom feigning, and non-forensic military samples have presented good effort on average (Nelson et al. 2010). Further, their removal from the meta-analysis resulted in a negligible change in the overall posterior mean effect size. However, without effort testing, the validity of cognitive performances within these studies remains unknown, which may have slightly impacted the effect sizes described within this meta-analysis.

The presence of trauma history within the population may have also influenced the observed effects of mTBI on cognition. Concussed soldiers with long-term cognitive complaints may suffer from trauma in addition to their mTBI; however, the current meta-analysis provided limited insight into the effects of PTSD on cognitive outcomes in cases of mTBI. Too few studies explored PTSD to effectively evaluate it as a moderator of injury. The non-significant correlation presented as largely underpowered and the PTSD effect sizes had a highly non-normal distribution. Overall, the PTSD effect sizes were quite high (see Table 1), aligning with past claims of high co-morbidity between mTBI and PTSD (Carlson et al. 2011; Chapman and Diaz-Arrastia 2014; French et al. 2011). As PTSD sequelae often interact with the sequelae of mTBI (Barth et al. 2010; Nelson et al. 2012; Shandera-Ochsner et al. 2013), it remains unclear whether the observed cognitive effect derives from the brain injury, the trauma associated with blast exposure, or an interaction between PTSD symptoms and the mTBI.

Notably, only one study identified in the systematic review involved a sample of non-military personnel exposed to blast injury (i.e., Baker et al. 2011). Evaluating blast-related mTBI

outside of the warzone, these authors identified negligible cognitive changes among Police Explosive Technicians following blast exposure through Forced Explosive Entry Training. In turn, exposure to the warzone and its associated traumas may have a greater impact on cognitive performances than blast-related mTBI. Even after controlling for stress, depression and the full spectrum of head injury, deployment in Iraq still presented statistically significant impairments on neuropsychological measures (Vasterling et al. 2006). The operational stress of deployment and the trauma element of injury in the warzone differentiate military mTBI from that of civilian concussion, but the current meta-analysis cannot shed light on the extent that trauma explains the chronic cognitive sequelae of mTBI among this population.

The meta-analysis was not only hindered by limited reporting of PTSD symptoms, but also by a small sample of studies in general. Few studies overall have evaluated the cognitive outcomes of blast-related mTBI and some constructs have very limited representation in the existing studies (see Table 2). As such, although the constructs shown to be sensitive to mTBI matched those hypothesized and proposed by past studies, some of the constructs that did not appear adversely affected by mTBI may simply have too few data points to calculate a posterior mean with a reasonably sized HDI. The current meta-analysis lacks sufficient data to make strong claims about the cognitive impact of mTBI on constructs with limited data points across studies (e.g., attention, motor, visuospatial skills). Moving forward, future researchers should explore these constructs in greater detail, as more observations may provide future meta-analysts with the power to identify any potential impairment in these constructs.

The few studies eligible for the meta-analysis also presented universally low study quality, as all studies drew inference from cross-sectional designs. Despite low study quality, a promising feature of the included studies was the standardized criteria of mTBI used as operational definitions by multiple authors. The majority of studies used the criteria established by the American Congress of Rehabilitation Medicine, while some authors provided alternative definitions. As researchers across all studies provided operational definitions of mTBI, the head injuries captured across studies has some level of commonality, which supports the validity of the current research synthesis at capturing the consequences of mTBI. Overcoming the limits of cross-sectional designs, the only study incorporating a longitudinal design to evaluate blast-related mTBI (Luethcke et al. 2011) did not meet eligibility criteria for the meta-analysis, as it only examined the acute effects of blast and non-blast mTBI within 72 h of injury. Although the study quality exceeded that of the cross-sectional designs included in the meta-analysis, the close proximity to injury would have biased the estimate of chronic effects of mTBI provided by the current meta-analysis, as the acute effects of mTBI appear much more severe (Karr et al. 2014a).

Moving forward, researchers with available data should enlist prospective designs with baseline testing that track blast-related mTBI past the acute phase of injury. The U.S. Department of Defense has already begun a program of universal baseline testing, using a specially designed computerized battery entitled the Automated Neuropsychological Assessment Metrics (ANAM; Seegmiller and Kane 2010). A handful of recent studies have evaluated cognitive change from baseline using the ANAM among military personnel suffering mTBI, but did not separately analyze blast-related injury (Bryan and Hernandez 2012; Kelly, Coldren, Parish, Dretsch, and Russell 2012; Roebuck-Spencer et al. 2012). Future designs should evaluate injury mechanism to identify if blast has a unique cognitive impact compared to blunt injuries. Further, increased testing occasions will allow for a clearer picture regarding cognitive change following blast-related mTBI, moving forward from cross-sectional research on the subtle, but chronic cognitive impairment associated with blast-related minor head injury.

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References

A reference marked with an asterisk indicates a study included in the meta-analysis.

*Amick, M.M., Clark, A., Fortier, C.B., Esterman, M., Rasmusson, A.M., Kenna, A., & McGlinchey, R. (2013). PTSD modifies performance on a task of affective executive control among deployed OEF/OIF veterans with mild traumatic brain injury. *Journal of the International Neuropsychological Society, 19*(7), 792–801. doi:10.1017/S1355617713000544.

Baker, A. J., Topolovec-Vranic, J., Michalak, A., Pollmann-Mudryj, M. A., Ouchterlony, D., Cheung, B., & Tien, H. C. (2011). Controlled blast exposure during forced explosive entry training and mild traumatic brain injury. *Journal of Trauma and Acute Care Surgery, 71*(5), S472–S477. doi:10.1097/TA.0b013e318232e7da.

Barth, J. T., Isler, W. C., Helmick, K. M., Wingler, I. M., & Jaffee, M. S. (2010). Acute battlefield assessment of concussion/mild TBI and return-to-duty evaluations. In C. H. Kennedy & J. L. Moore (Eds.), *Military neuropsychology* (pp. 29–55). New York: Springer Publishing Co.

Bauman, R. A., Ling, G., Tong, L., Januszkiewicz, A., Agoston, D., Delanerolle, N., & Parks, S. (2009). An introductory characterization of a combat-casualty-care relevant swine model of closed head injury resulting from exposure to explosive blast. *Journal of Neurotrauma, 26*(6), 841–860. doi:10.1089/neu. 2009.0898.

Bazarian, J., Donnelly, K., Peterson, D., Warner, G., Zhu, T., & Zhong, J. (2013). The relation between posttraumatic stress disorder and mild traumatic brain injury acquired during Operations Enduring Freedom and Iraqi Freedom. *The Journal of Head Trauma Rehabilitation, 28*(1), 1–12. doi:10.1097/HTR.0b013e318256d3d3.

Belanger, H. G., Kretzmer, T., Yoash-Gantz, R., Pickett, T., & Tupler, L. A. (2009). Cognitive sequelae of blast-related versus other mechanisms of brain trauma. *Journal of the International Neuropsychological Society, 15*(1), 1–8. doi:10.1017/S1355617708090036.

Belanger, H. G., Spiegel, E., & Vanderploeg, R. (2010). Neuropsychological performance following a history of multiple self-reported concussions: A meta-analysis. *Journal of the International Neuropsychological Society, 16*(2), 262–267. doi:10.1017/S1355617709991287.

Belanger, H. G., Proctor-Weber, Z., Kretzmer, T., Kim, M., French, L. M., & Vanderploeg, R. D. (2011). Symptom complaints following reports of blast versus non-blast mild TBI: Does mechanism of injury matter? *The Clinical Neuropsychologist, 25*(5), 702–715. doi:10.1080/13854046.2011.566892.

Belanger, H. G., Curtiss, G., Demery, J. A., Lebowitz, B. K., & Vanderploeg, R. D. (2005). Factors moderating neuropsychological outcomes following mild traumatic brain injury: A meta-analysis. *Journal of the International Neuropsychological Society, 11*(3), 215–227. doi:10.10170S1355617705050277..

Belanger, H. G., & Vanderploeg, R. D. (2005). The neuropsychological impact of sports-related concussion: A meta-analysis. *Journal of the International Neuropsychological Society, 11*(4), 345–357.

Belanger, H., Vanderploeg, R., Curtiss, G., & Warden, D. (2007). Recent neuroimaging techniques in mild traumatic brain injury. *The Journal of Neuropsychiatry and Clinical Neurosciences, 19*(1), 5–20.

Benzinger, T. L., Brody, D., Cardin, S., Curley, K. C., Mintun, M. A., Mun, S. K., & Wrathall, J. R. (2009). Blast-related brain injury: Imaging for clinical and research applications: Report of the 2008 St. Louis workshop. *Journal of Neurotrauma, 26*(12), 2127–2144. doi:10.1089/neu.2009.0885.

Binder, L. M., Rohling, M. L., & Larrabee, G. J. (1997). A review of mild head trauma: I. Meta-analytic review of neuropsychological studies. *Journal of Clinical and Experimental Neuropsychology, 19*(3), 421–431. doi:10.1080/01688639708403870.

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S., & Keane, T. M. (1995). The development of a clinician-administered PTSD scale. *Journal of Traumatic Stress, 8*, 75–90. doi:10.1002/jts.2490080106.

Bogdanova, Y., & Verfaellie, M. (2012). Cognitive sequelae of blast-induced traumatic brain injury: Recovery and rehabilitation. *Neuropsychology Review, 22*(1), 4–20. doi:10.1007/s11065-012-9192-3.

Bryan, C., & Hernandez, A. M. (2012). Magnitudes of decline on automated neuropsychological assessment metrics subtest scores relative to predeployment baseline performance among service members evaluated for traumatic brain injury in Iraq. *The Journal of Head Trauma Rehabilitation, 27*(1), 45–54. doi:10.1097/HTR.0b013e318238f146.

Bryant, R. (2011). Post-traumatic stress disorder vs traumatic brain injury. *Dialogues in Clinical Neuroscience, 13*(3), 251–262.

Cabeza, R., & Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience, 12*(1), 1–47. doi:10.1162/08989290051137585.

Carlson, K. F., Kehle, S. M., Meis, L. A., Greer, N., MacDonald, R., Rutks, I., & Wilt, T. J. (2011). Prevalence, assessment, and treatment of mild traumatic brain injury and posttraumatic stress disorder: A systematic review of the evidence. *The Journal of Head Trauma Rehabilitation, 26*(2), 103–115.

Cernak, I., & Noble-Haeusslein, L. J. (2010). Traumatic brain injury: An overview of pathobiology with emphasis on military populations. *Journal of Cerebral Blood Flow & Metabolism, 30*(2), 255–266. doi:10.1038/jcbfm.2009.203.

Chapman, J. C., & Diaz-Arrastia, R. (2014). Military traumatic brain injury: A review. *Alzheimer's & Dementia, 10*(3), S97–S104. doi:10.1016/j.jalz.2014.04.012.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale: Lawrence Erlbaum Associates.

Comper, P., Hutchison, M., Magrys, S., Mainwaring, L., & Richards, D. (2010). Evaluating the methodological quality of sports neuropsychology concussion research: A systematic review. *Brain Injury, 24*(11), 1257–1271. doi:10.3109/02699052.2010.506854.

Cooper, D. B., Chau, P. M., Armistead-Jehle, P., Vanderploeg, R. D., & Bowles, A. O. (2012). Relationship between mechanism of injury and neurocognitive functioning in OEF/OIF service members with mild traumatic brain injuries. *Military Medicine, 177*(10), 1157–1160. doi:10.7205/MILMED-D-12-00098.

Dobie, D. J., Kivlahan, D. R., Maynard, C., Bush, K. R., McFall, M. E., Epler, A. J., & Bradley, K. A. (2002). Screening for posttraumatic stress disorder in female Veteran's Affairs patients: Validation of the PTSD Checklist. *General Hospital Psychiatry, 24*, 367–374.

Dolan, S., Martindale, S., Robinson, J., Kimbrel, N. A., Meyer, E. C., Kruse, M. I., & Gulliver, S. B. (2012). Neuropsychological sequelae of PTSD and TBI following war deployment among OEF/OIF veterans. *Neuropsychology Review, 22*(1), 21–34. doi:10.1007/s11065-012-9190-5.

Dougan, B. K., Horswill, M. S., & Geffen, G. M. (2013). Athletes' age, sex, and years of education moderate the acute neuropsychological impact of sports-related concussion: A meta-analysis. *Journal of the International Neuropsychological Society, 19*, 1–17.

Eierud, C., Craddock, R. C., Fletcher, S., Aulakh, M., King-Casas, B., Kuehl, D., & LaConte, S. M. (2014). Neuroimaging after mild traumatic brain injury: Review and meta-analysis. *NeuroImage: Clinical, 4*, 283–294. doi:10.1016/j.nicl.2013.12.009.

Fortier, C. B., Amick, M. M., Grande, L., McGlynn, S., Kenna, A., Morra, L., & McGlinchey, R. E. (2014). The Boston assessment of traumatic brain injury–lifetime (BAT-L) semistructured interview: Evidence of research utility and validity. *The Journal of Head Trauma Rehabilitation, 29*(1), 89–98. doi:10.1097/HTR.0b013e3182865859.

French, L. M., Iverson, G. L., Lange, R. T., & Bryant, R. A. (2011). Neuropsychological consequences of injury in military personnel. In S. S. Bush & G. L. Iverson (Eds.), *Neuropsychological assessment of work-related injuries* (pp. 127–160). New York: The Guilford Press.

Frencham, K. A., Fox, A. M., & Maybery, M. (2005). Neuropsychological studies of mild traumatic brain injury: A meta-analytic review of research since 1995. *Journal of Clinical and Experimental Neuropsychology, 27*(3), 334–351.

Gavett, B. E., Stern, R. A., & McKee, A. C. (2011). Chronic traumatic encephalopathy: A potential late effect of sport-related concussive and subconcussive head trauma. *Clinics in Sports Medicine, 30*, 179–188. doi:10.1016/j.csm.2010.09.007.

Gelman, A. (2006). Prior distributions for variance parameters in hierarchical models. *Bayesian Analysis, 1*(3), 515–534.

Goldstein, L., Fisher, A., Tagge, C., Zhang, X., Velisek, L., Sullivan, J., & McKee, A. (2012). Chronic traumatic encephalopathy in blast-exposed military veterans and a blast neurotrauma mouse model. *Science Translational Medicine, 4*(134), 134ra60. doi:10.1126/scitranslmed.3003716.

Gondusky, J. S., & Reiter, M. P. (2005). Protecting military convoys in Iraq: An examination of battle injuries sustained by a mechanized battalion during Operation Iraqi Freedom II. *Military Medicine, 170*(6), 546–549.

Greiffenstein, M. F. (2010). Noncredible neuropsychological presentation in service members and veterans. In C. H. Kennedy & J. L. Moore (Eds.), *Military neuropsychology* (pp. 81–100). New York: Springer Publishing Co.

Greiffenstein, M. F., & Baker, W. J. (2008). Validity testing in dually diagnosed post-traumatic stress disorder and mild closed head injury. *The Clinical Neuropsychologist, 22*(3), 565–582.

Gunning-Dixon, F. M., & Raz, N. (2000). The cognitive correlates of white matter abnormalities in normal aging: A quantitative

review. *Neuropsychology, 14*(2), 224–232. doi:10.1037/0894-4105.14.2.224.

Guskiewicz, K., Marshall, S., Bailes, J., McCrea, M., Cantu, R., Randolph, C., & Jordan, B. (2005). Association between recurrent concussion and late-life cognitive impairment in retired professional football players. *Neurosurgery, 57*, 719–726. doi:10.1227/01.NEU.0000175725.75780.DD.

Halterman, C. I., Langan, J., Drew, A., Rodriguez, E., Osternig, L. R., Chou, L. S., & Van Donkelaar, P. (2006). Tracking the recovery of visuospatial attention deficits in mild traumatic brain injury. *Brain, 129*(3), 747–753.

Hayes, J., Morey, R., & Tupler, L. (2012). A case of frontal neuropsychological and neuroimaging signs following multiple primary-blast exposure. *Neurocase, 18*(3), 258–269. doi:10.1080/13554794.2011.588181.

Hayward, P. (2008). Traumatic brain injury: The signature of modern conflicts. *The Lancet Neurology, 7*, 200–201. doi:10.1016/S1474-4422(08)70032-2.

Hoge, C. W., McGurk, D., Thomas, J. L., Cox, A. L., Engel, C. C., & Castro, C. A. (2008). Mild traumatic brain injury in US soldiers returning from Iraq. *New England Journal of Medicine, 358*(5), 453–463. doi:10.1056/NEJMoa072972.

Hurley, R. A., McGowan, J. C., Arfanakis, K., & Taber, K. H. (2004). Traumatic axonal injury: Novel insights into evolution and identification. *The Journal of Neuropsychiatry and Clinical Neurosciences, 16*(1), 1–7. doi:10.1176/appi.neuropsych.16.1.1.

Jorge, R., Acion, L., White, T., Tordesillas-Gutierrez, D., Pierson, R., Crespo-Facorro, B., & Magnotta, V. (2012). White matter abnormalities in veterans with mild traumatic brain injury. *The American Journal of Psychiatry, 169*(12), 1284–1291. doi:10.1176/appi.ajp.2012.12050600.

Karantzoulis, S., & Randolph, C. (2013). Modern chronic traumatic encephalopathy in retired athletes: What is the evidence? *Neuropsychology Review, 23*(4), 350–360. doi:10.1007/s11065-013-9243-4.

Karr, J. E., Areshenkoff, C. N., & Garcia-Barrera, M. A. (2014a). The neuropsychological outcomes of concussion: A systematic review of meta-analyses on the cognitive sequelae of mild traumatic brain injury. *Neuropsychology, 28*(3), 321–336. doi:10.1037/neu0000037.

Karr, J. E., Garcia-Barrera, M. A., & Areshenkoff, C. N. (2014b). Executive functions and intra-individual variability following concussion. *Journal of Clinical and Experimental Neuropsychology, 36*(1), 15–31. doi:10.1080/13803395.2013.863833.

Kelly, M. P., Coldren, R. L., Parish, R. V., Dretsch, M. N., & Russell, M. L. (2012). Assessment of acute concussion in the combat environment. *Archives of Clinical Neuropsychology, 27*(4), 375–388. doi:10.1093/arclin/acs036.

Khachaturian, A. S., & Khachaturian, Z. S. (2014). Military risk factors for Alzheimer's dementia and neurodegenerative disease. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association, 10*(3), S90–S91. doi:10.1016/j.jalz.2014.05.1085.

Kocsis, J. D., & Tessler, A. (2009). Pathology of blast-related brain injury. *Journal of Rehabilitation Research and Development, 46*(6), 667–672. doi:10.1682/JRRD.2008.08.0100.

Koliatsos, V. E., Cernak, I., Xu, L., Song, Y., Savonenko, A., Crain, B. J., & Lee, D. (2011). A mouse model of blast injury to brain: Initial pathological, neuropathological, and behavioral characterization. *Journal of Neuropathology & Experimental Neurology, 70*(5), 399–416. doi:10.1097/NEN.0b013e3182189f06.

*Kontos, A.P., Kotwal, R.S., Elbin, R.J., Lutz, R.H., Forsten, R.D., Benson, P.J., & Guskiewicz, K.M. (2013). Residual effects of combat-related mild traumatic brain injury. *Journal of Neurotrauma, 30*(8), 680–686. doi:10.1089/neu.2012.2506.

Lange, R. T., Pancholi, S., Brickell, T. A., Sakura, S., Bhagwat, A., Merritt, V., & French, L. M. (2012). Neuropsychological outcome from blast versus non-blast: Mild traumatic brain injury in U.S. military service members. *Journal of the International Neuropsychological Society, 18*(3), 595–605. doi:10.1017/S1355617712000239.

Lee, R. R., & Huang, M. (2014). Magnetoencephalography in the diagnosis of concussion. *Progress in Neurological Surgery, 28*, 94–111. doi:10.1159/000358768.

Lehman, E. J., Hein, M., Baron, S., & Gersic, C. (2012). Neurodegenerative causes of death among retired national football league players. *Neurology, 79*, 1970–1974. doi:10.1212/WNL.0b013e31826daf50.

Leung, L. Y., VandeVord, P. J., Dal Cengio, A. L., Bir, C., Yang, K. H., & King, A. I. (2008). Blast related neurotrauma: A review of cellular injury. *Molecular & Cellular Biomechanics, 5*(3), 155–168.

Levin, H., Wilde, E., Troyanskaya, M., Petersen, N., Scheibel, R., Newsome, M., & Li, X. (2010). Diffusion tensor imaging of mild to moderate blast-related traumatic brain injury and its sequelae. *Journal of Neurotrauma, 27*(4), 683–694. doi:10.1089/neu.2009.1073.

Lew, H., Thomander, D., Chew, K., & Bleiberg, J. (2007). Review of sports-related concussion: Potential for application in military settings. *Journal of Rehabilitation Research and Development, 44*(7), 963–973. doi:10.1682/JRRD.2006.12.0169.

Lew, H. L., Vanderploeg, R. D., Moore, D. F., Schwab, K., Friedman, L., Yesavage, J., & Sigford, B. J. (2008). Overlap of mild TBI and mental health conditions in returning OIF/OEF service members and veterans. *Journal of Rehabilitation Research and Development, 45*(3), xi–xvi. doi:10.1682/JRRD.2008.05.0064.

Lippa, S. M., Pastorek, N. J., Benge, J. F., & Thornton, G. (2010). Postconcussive symptoms after blast and nonblast-related mild traumatic brain injuries in Afghanistan and Iraq war veterans. *Journal of the International Neuropsychological Society, 16*(5), 856–866. doi:10.1017/S1355617710000743.

Lipton, M., Gulko, E., Zimmerman, M., Friedman, B., Kim, M., Gellella, E., & Branch, C. (2009). Diffusion-tensor imaging implicates prefrontal axonal injury in executive function impairment following very mild traumatic brain injury. *Radiology, 252*(3), 816–824. doi:10.1148/radiol.2523081584.

Luethcke, C. A., Bryan, C. J., Morrow, C. E., & Isler, W. C. (2011). Comparison of concussive symptoms, cognitive performance, and psychological symptoms between acute blast-versus nonblast-induced mild traumatic brain injury. *Journal of the International Neuropsychological Society, 17*(1), 36–45. doi:10.1017/S1355617710001207.

Mac Donald, C., Johnson, A., Cooper, D., Malone, T., Sorrell, J., Shimony, J., & Brody, D. (2013). Cerebellar white matter abnormalities following primary blast injury in US military personnel. *PLoS ONE, 8*(2), e55823. doi:10.1371/journal.pone.0055823.

Mac Donald, C., Johnson, A., Cooper, D., Nelson, E., Werner, N., Shimony, J., & Brody, D. (2011). Detection of blast-related traumatic brain injury in U.S. military personnel. *The New England Journal of Medicine, 364*(22), 2091–2100. doi:10.1056/NEJMoa1008069.

MacGregor, A., Dougherty, A., & Galarneau, M. (2011). Injury-specific correlates of combat-related traumatic brain injury in Operation Iraqi Freedom. *The Journal of Head Trauma Rehabilitation, 26*(4), 312–318. doi:10.1097/HTR.0b013e3181e94404.

Matthews, S. C., Spadoni, A. D., Lohr, J. B., Strigo, I. A., & Simmons, A. N. (2012). Diffusion tensor imaging evidence of white matter disruption associated with loss versus alteration of consciousness in warfighters exposed to combat in Operations Enduring and Iraqi Freedom. *Psychiatry Research: Neuroimaging, 204*(2–3), 149–154. doi:10.1016/j.pscychresns.2012.04.018.

Matthews, S. C., Strigo, I. A., Simmons, A. N., O'Connell, R. M., Reinhardt, L. E., & Moseley, S. A. (2011). A multimodal imaging study in U.S. veterans of Operations Iraqi and Enduring Freedom with and without major depression after blast-related concussion. *NeuroImage, 54*(Suppl 1), S69–S75. doi:10.1016/j.neuroimage.2010.04.269.

Mayer, A. R., Mannell, M. V., Ling, J., Gasparovic, C., & Yeo, R. A. (2011). Functional connectivity in mild traumatic brain injury. *Human Brain Mapping, 32*(11), 1825–1835. doi:10.1002/hbm.21151.

McCrory, P., Meeuwisse, W. H., Aubry, M., Cantu, B., Dvořák, J., Echemendia, R. J., & Turner, M. (2013). Consensus statement on concussion in sport: The 4th international conference on concussion in sport held in Zurich, November 2012. *British Journal of Sports Medicine, 47*(5), 250–258. doi:10.1136/bjsports-2013-092313.

McKee, A. C., Cantu, R., Nowinski, C., Hedley-Whyte, E., Gavett, B., Budson, A., & Stern, R. (2009). Chronic traumatic encephalopathy in athletes: Progressive tauopathy after repetitive head injury. *Journal of Neuropathology and Experimental Neurology, 68*, 709–735. doi:10.1097/NEN.0b013e3181a9d503.

McKee, A. C., Stein, T. D., Nowinski, C. J., Stern, R. A., Daneshvar, D. H., Alvarez, V. E., & Cantu, R. C. (2013). The spectrum of disease in chronic traumatic encephalopathy. *Brain, 136*(1), 43–64. doi:10.1093/brain/aws307.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41*(1), 49–100. doi:10.1006/cogp.1999.0734.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D., & the PRISMA Group. (2009). Preferred reporting items for systematic reviews and metaanalyses: The PRISMA statement. *Annals of Internal Medicine, 151*, 264–269. doi:10.7326/0003-4819-151-4-200908180-00135.

Mori, S., & Zhang, J. (2006). Principles of diffusion tensor imaging and its applications to basic neuroscience research. *Neuron, 51*(5), 527–539. doi:10.1016/j.neuron.2006.08.012.

Murray, C. K., Reynolds, J. C., Schroeder, J. M., Harrison, M. B., Evans, O. M., & Hospenthal, D. R. (2005). Spectrum of care provided at an Echelon II medical unit during Operation Iraqi Freedom. *Military Medicine, 170*(6), 516–520.

*Nelson, N.W., Hoelzle, J.B., Doane, B.M., McGuire, K.A., Ferrier-Auerbach, A.G., Charlesworth, M.J, & Sponheim, S.R. (2012). Neuropsychological outcomes of US veterans with report of remote blast-related concussion and current psychopathology. *Journal of the International Neuropsychological Society, 18*(5), 845–855. doi:10.1017/S1355617712000616.

*Nelson, N.W., Hoelzle, J.B., McGuire, K.A., Ferrier-Auerbach, A.G., Charlesworth, M.J., & Sponheim, S.R. (2010). Evaluation context impacts neuropsychological performance of OEF/OIF veterans with reported combat-related concussion. *Archives of Clinical Neuropsychology, 25*, 713–723. doi:10.1093/arclin/acq075.

Niogi, S., & Mukherjee, P. (2010). Diffusion tensor imaging of mild traumatic brain injury. *The Journal of Head Trauma Rehabilitation, 25*(4), 241–255. doi:10.1097/HTR.0b013e3181e52c2a.

Niogi, S. N., Mukherjee, P., Ghajar, J., Johnson, C. E., Kolster, R., Lee, H., & McCandliss, B. D. (2008). Structural dissociation of attentional control and memory in adults with and without mild traumatic brain injury. *Brain, 131*(12), 3209–3221.

OCEBM (Oxford Centre for Evidence-Based Medicine) Levels of Evidence Working Group. (2011). *The Oxford Levels of Evidence 2.* Retrieved from http://www.cebm.net/index.aspx?o=5653.

Okie, S. (2005). Traumatic brain injury in the war zone. *New England Journal of Medicine, 352*(20), 2043–2047. doi:10.1056/NEJMp058102.

Omalu, B., Hammers, J. L., Bailes, J., Hamilton, R. L., Kamboh, M. I., Webster, G., & Fitzsimmons, R. P. (2011). Chronic traumatic encephalopathy in an Iraqi war veteran with posttraumatic stress disorder who committed suicide. *Neurosurgical Focus, 31*(5), E3. doi:10.3171/2011.9.FOCUS11178.

Owens, B. D., Kragh, J. F., Jr., Wenke, J. C., Macaitis, J., Wade, C. E., & Holcomb, J. B. (2008). Combat wounds in operation Iraqi Freedom and operation Enduring Freedom. *The Journal of Trauma: Injury, Infection, and Critical Care, 64*(2), 295–299. doi:10.1097/TA.0b013e318163b875.

Packwood, S., Hodgetts, H. M., & Tremblay, S. (2011). A multiperspective approach to the conceptualization of executive functions. *Journal of Clinical and Experimental Neuropsychology, 33*(4), 456–470. doi:10.1080/13803395.2010.533157.

Pertab, J. L., James, K. M., & Bigler, E. (2009). Limitations of mild traumatic brain injury meta-analyses. *Brain Injury, 23*(6), 498–508.

*Peskind, E.R., Petrie, E.C., Cross, D.J., Pagulayan, K., McCraw, K., Hoff, D., & Minoshima, S. (2011). Cerebrocerebellar hypometabolism associated with repetitive blast exposure mild traumatic brain injury in 12 Iraq war Veterans with persistent post-concussive symptoms. *Neuroimage, 54*, S76–S82. doi:10.1016/j.neuroimage.2010.04.008.

Petrie, E., Cross, D., Yarnykh, V., Richards, T., Martin, N., Pagulayan, K., & Peskind, E. (2014). Neuroimaging, behavioral, and psychological sequelae of repetitive combined blast/impact mild traumatic brain injury in Iraq and Afghanistan war veterans. *Journal of Neurotrauma, 31*(5), 425–436. doi:10.1089/neu.2013.2952.

Pietrzak, R. H., Johnson, D. C., Goldstein, M. B., Malley, J. C., & Southwick, S. M. (2009). Posttraumatic stress disorder mediates the relationship between mild traumatic brain injury and health and psychosocial functioning in veterans of Operations Enduring Freedom and Iraqi Freedom. *The Journal of Nervous and Mental Disease, 197*(10), 748–753. doi:10.1097/NMD.0b013e3181b97a75.

Posner, M. I., & Rothbart, M. K. (2007). Research on attention networks as a model for the integration of psychological science. *Annual Review of Psychology, 58*, 1–23. doi:10.1146/annurev.psych.58.110405.085516.

Posner, M. I., Rothbart, M. K., Sheese, B. E., & Tang, Y. (2007). The anterior cingulate gyrus and the mechanism of self-regulation. *Cognitive, Affective, & Behavioral Neuroscience, 7*(4), 391–395. doi:10.3758/CABN.7.4.391.

Prigatano, G. P., & Borgaro, S. R. (2006). Neuropsychological testing after traumatic brain injury. In R. W. Evans (Ed.), *Neurology and trauma* (2nd ed., pp. 230–237). New York: Oxford University Press.

Development Core Team, R. (2008). *R: A language and environment for statistical computing*. Vienna: R Foundation for Statistical Computing.

Roebuck-Spencer, T. M., Vincent, A. S., Twillie, D. A., Logan, B. W., Lopez, M., Friedl, K. E., & Kirby, G. (2012). Cognitive change associated with self-reported mild traumatic brain injury sustained during the OEF/OIF conflicts. *The Clinical Neuropsychologist, 26*(3), 473–489. doi:10.1080/13854046.2011.650214.

Rohling, M. L., Binder, L. M., Demakis, G. J., Larrabee, G. J., Ploetz, D. M., & Langhinrichsen-Rohling, J. (2011). A meta-analysis of neuropsychological outcome after mild traumatic brain injury: Re-analyses and reconsiderations of Binder et al. (1997), Frencham et al. (2005), and Pertab et al. (2009). *The Clinical Neuropsychologist, 25*(4), 608–623. doi:10.1080/13854046.2011.565076.

Rosenfeld, J. V., McFarlane, A. C., Bragge, P., Armonda, R. A., Grimes, J. B., & Ling, G. S. (2013). Blast-related traumatic brain injury. *The Lancet Neurology, 12*(9), 882–893.

Rustemeyer, J., Kranz, V., & Bremerich, A. (2007). Injuries in combat from 1982–2005 with particular reference to those to the head and neck: A review. *British Journal of Oral and Maxillofacial Surgery, 45*(7), 556–560. doi:10.1016/j.bjoms.2007.01.003.

*Scheibel, R.S., Newsome, M.R., Troyanskaya, M., Lin, X., Steinberg, J.L., Radaideh, M., & Levin, H.S. (2012). Altered brain activation in military personnel with one or more traumatic brain injuries following blast. *Journal of the International Neuropsychological Society, 18*(1), 89–100. doi:10.1017/S1355617711001433.

Schreiber, S., Barkai, G., Gur-Hartman, T., Peles, E., Tov, N., Dolberg, O. T., & Pick, C. G. (2008). Long-lasting sleep patterns of adult patients

with minor traumatic brain injury (mTBI) and non-mTBI subjects. *Sleep Medicine, 9*(5), 481–487. doi:10.1016/j.sleep.2007.04.014.

Schretlen, D. J., & Shapiro, A. (2003). A quantitative review of the effects of traumatic brain injury on cognitive functioning. *International Review of Psychiatry, 15*(4), 341–349. doi:10.1080/0954026031000160672 8.

Seegmiller, R. A., & Kane, R. L. (2010). The future of military neuropsychology. In C. H. Kennedy & J. L. Moore (Eds.), *Military neuropsychology* (pp. 383–404). New York: Springer Publishing Co.

*Shandera-Ochsner, A.L., Berry, D.T., Harp, J.P., Edmundson, M., Graue, L. O., Roach, A., & High Jr, W.M. (2013). Neuropsychological Effects of Self-Reported Deployment-Related Mild TBI and Current PTSD in OIF/OEF Veterans. *The Clinical Neuropsychologist, 27*(6), 881–907. doi:10.1080/13854046.2013.802017.

Shenton, M. E., Hamoda, H. M., Schneiderman, J. S., Bouix, S., Pasternak, O., Rathi, Y., & Zafonte, R. (2012). A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury. *Brain Imaging and Behavior, 6*(2), 137–192. doi:10.1007/s11682-012-9156-5.

Sibener, L., Zaganjor, I., Snyder, H. M., Bain, L. J., Egge, R., & Carrillo, M. C. (2014). Alzheimer's Disease prevalence, costs, and prevention for military personnel and veterans. *Alzheimer's & Dementia, 10*(3), S105–S110. doi:10.1016/j.jalz.2014.04.011.

Sorg, S. F., Delano-Wood, L., Luc, N., Schiehser, D. M., Hanson, K. L., Nation, D. A., & Bondi, M. W. (2014). White matter integrity in veterans with mild traumatic brain injury: Associations with executive function and loss of consciousness. *The Journal of Head Trauma Rehabilitation, 29*(1), 21–32. doi:10.1097/HTR.0b013e31828a1aa4.

Sosnoff, J. J., Broglio, S. P., Hillman, C. H., & Ferrara, M. S. (2007). Concussion does not impact intraindividual response time variability. *Neuropsychology, 21*(6), 796–802. doi:10.1037/0894-4105.21.6.796.

Sponheim, S., McGuire, K., Kang, S., Davenport, N., Aviyente, S., Bernat, E., & Lim, K. (2011). Evidence of disrupted functional connectivity in the brain after combat-related blast injury. *NeuroImage, 54*(Suppl 1), S21–S29. doi:10.1016/j.neuroimage.2010.09.007.

Stan Development Team. (2014). RStan: The R interface to Stan (Version 2.3) [Computer software]. http://mc-stan.org/rstan.html.

Sutton, A. J., & Abrams, K. R. (2001). Bayesian methods in meta-analysis and evidence synthesis. *Statistical Methods in Medical Research, 10*(4), 277–303. doi:10.1177/096228020101000404.

Tanielian, T. L., & Jaycox, L. (Eds.). (2008). *Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery.* Santa Monica: Rand Corporation.

Thornton, A., & Lee, P. (2000). Publication bias in meta-analysis: Its causes and consequences. *Journal of Clinical Epidemiology, 53*(2), 207–216. doi:10.1016/S0895-4356(99)00161-4.

U.S. Department of Defense. (2014). *DoD TBI Worldwide Numbers since 2000*. Retrieved from http://dvbic.dcoe.mil/sites/default/files/uploads/Worldwide%20Totals%202000-2014Q1.pdf.

Vanderploeg, R. D., & Schinka, J. A. (2004). Estimation of premorbid cognitive abilities: Issues and approaches. In J. H. Ricker (Ed.), *Differential diagnosis in adult neuropsychological assessment* (pp. 27–65). New York: Springer Publishing Company.

*Vakhtin, A.A., Calhoun, V.D., Jung, R.E., Prestopnik, J.L., Taylor, P.A., & Ford, C.C. (2013). Changes in intrinsic functional brain networks following blast-induced mild traumatic brain injury. *Brain Injury, 27*(11), 1304–1310. doi:10.3109/02699052.2013.823561.

Vasterling, J. J., & Dikmen, S. (2012). Mild traumatic brain injury and posttraumatic stress disorder: Clinical and conceptual complexities. *Journal of the International Neuropsychological Society, 18*(3), 390–393. doi:10.1017/S1355617712000367.

Vasterling, J. J., Proctor, S. P., Amoroso, P., Kane, R., Heeren, T., & White, R. F. (2006). Neuropsychological outcomes of army personnel following deployment to the Iraq war. *The Journal of the American Medical Association, 296*(5), 519–529. doi:10.1001/jama.296.5.519.

Verfaellie, M., Lafleche, G., Spiro, A., III, & Bousquet, K. (2014). Neuropsychological outcomes in OEF/OIF veterans with self-report of blast exposure: Associations with mental health, but not MTBI. *Neuropsychology, 28*(3), 337–346. doi:10.1037/neu0000027.

Wilk, J. E., Thomas, J. L., McGurk, D. M., Riviere, L. A., Castro, C. A., & Hoge, C. W. (2010). Mild traumatic brain injury (concussion) during combat: Lack of association of blast mechanism with persistent postconcussive symptoms. *The Journal of Head Trauma Rehabilitation, 25*(1), 9–14. doi:10.1097/HTR.0b013e3181bd090f.

Witt, S. T., Lovejoy, D. W., Pearlson, G. D., & Stevens, M. C. (2010). Decreased prefrontal cortex activity in mild traumatic brain injury during performance of an auditory oddball task. *Brain Imaging and Behavior, 4*(3–4), 232–247. doi:10.1007/s11682-010-9102-3.

Xydakis, M. S., Fravell, M. D., Nasser, K. E., & Casler, J. D. (2005). Analysis of battlefield head and neck injuries in Iraq and Afghanistan. *Otolaryngology-Head and Neck Surgery, 133*(4), 497–504. doi:10.1016/j.otohns.2005.07.003.

Yeh, P. H., Wang, B., Oakes, T. R., French, L. M., Pan, H., Graner, J., & Riedy, G. (2014). Postconcussional disorder and PTSD symptoms of military-related traumatic brain injury associated with compromised neurocircuitry. *Human Brain Mapping, 35*(6), 2652–2673. doi:10.1002/hbm.22358.

Zakzanis, K. K., Leach, L., & Kaplan, E. (1999). Mild traumatic brain injury. In K. K. Zakzanis, L. Leach, & E. Kaplan (Eds.), *Neuropsychological differential diagnosis* (pp. 163–171). Lisse Netherlands: Swets & Zeitlinger Publishers.