

# The Neuropsychological Outcomes of Concussion: A Systematic Review of Meta-Analyses on the Cognitive Sequelae of Mild Traumatic Brain Injury

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Mild Traumatic Brain Injury (mTBI), also known as concussion, has become a growing public health concern, prevalent in both athletic and military settings. Many researchers have examined post-mTBI neuropsychological outcomes, leading to multiple meta-analyses amalgamating individual study results. **Objective:** Considering the plethora of meta-analytic findings, the next logical step stands as a systematic review of meta-analyses, effectively reporting key moderators that predict post-mTBI neuropsychological outcomes. **Method:** A systematic review of reviews yielded 11 meta-analyses meeting inclusion criteria (i.e., English-language systematic reviews/meta-analyses covering post-mTBI observational cognitive research on late adolescents/adults), with their findings qualitatively synthesized based on moderator variables (i.e., cognitive domain, time since injury, past head injury, participant characteristics, comparison group, assessment technique, and persistent symptoms). **Results:** The overall effect sizes ranged for both general (range: .07–.61) and sports-related mTBI (range: .40–.81) and differed both between and within cognitive domains, with executive functions appearing most sensitive to multiple mTBI. Cognitive domains varied in recovery rates, but overall recovery occurred by 90 days postinjury for most individuals and by 7 days postinjury for athletes. Greater age/education and male gender produced smaller effects sizes, and high school athletes suffered the largest deficits post-mTBI. Control-group comparisons yielded larger effects than within-person designs, and assessment techniques had limited moderating effects. **Conclusions:** Overall, meta-analytic review quality remained low with few studies assessing publication or study quality bias. Meta-analyses consistently identified adverse acute mTBI-related effects and fairly rapid symptom resolution. Future meta-analyses should better operationally define cognitive constructs to produce more consistent effect estimates across domains.

**Keywords:** mTBI, concussion, mild traumatic brain injury, cognition, neuropsychology

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Mild Traumatic Brain Injury (mTBI), also known as concussion, stands as a prevalent neurotrauma within the general population (Cassidy et al., 2004), increasingly common in both athletic (Coronado, McGuire, Faul, Sugerman, & Pearson, 2012) and military settings (Iverson, Langlois, McCrea, & Kelly, 2009). The rates and consequences of mTBI have become progressively more publicized, both in sports (Moser, 2007) and in modern conflicts (Hayward, 2008). Highly prevalent in American football (Gessel,

Fields, Collins, Dick, & Comstock, 2007), mTBI now represents a signature injury of the sport. Although its seriousness has been historically underestimated, repeated mTBIs among young athletes have been linked to significant neurodegeneration long after retiring from play (Gavett, Stern, & McKee, 2011; Guskiewicz et al., 2005; McKee et al., 2009). In 2011, Dave Duerson, a former American football safety, took his own life after years of cognitive and emotional complaints that he attributed to past concussions. Duerson donated his brain to science, and neurologist Amy McKee identified substantial abnormalities in his frontal cortex, showing longstanding neural atrophy potentially related to repeated mTBI (Roehr, 2012). Amplifying the consequences shown in Duerson's case, professional American football players present three times the likelihood of neurodegenerative mortality than the general population (Lehman, Hein, Baron, & Gersic, 2012). With the apparent neurological damage associated with mTBI, the prevalence of this common neurotrauma presents an ever more worrisome context.

In the United States, TBI results in \$60 billion in the total lifetime costs of injury (Finkelstein, Corso, & Miller, 2006), with the majority of these traumas categorized as mild (Cassidy et al., 2004). Although underestimated due to unreported injury rates, the prevalence of mTBI may stand as high as 600 cases per 100,000 people (Cassidy et al., 2004). Mixed-mechanism mTBI characterizes the injury among the general population (e.g., falls, motor

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vehicle accidents; Ropper & Gorson, 2007); however, brain injuries occur at an alarming frequency among athletes, with sports-related TBI rates potentially twice that of TBI rates in the general population (Coronado et al., 2012). Approximately, 1.6 to 3.8 million sports-related TBIs occur annually; however, this estimate may remain low due to unreported or unrecognized cases (Langlois, Rutland-Brown, & Wald, 2006). Among American intercollegiate athletes, mTBIs accounted for 6.2% of all sports-related injuries, with contact sports (e.g., lacrosse, football, soccer) presenting the highest risks (Covassin, Swanik, & Sachs, 2003). Football accounted for 55% of all concussions recorded across 16 years of injury surveillance, and women's soccer and ice hockey presented disconcertingly high concussion rates (i.e., .41 and .91 per 1,000 athlete-exposures, respectively; Hootman, Dick, & Agel, 2007). Across all high school sports, 2.5 concussions occur for every 10,000 games and practices (Guerriero, Proctor, Mannix, & Meehan, 2012) with American football presenting the most cases of mTBI (Coronado et al., 2012; Gessel et al., 2007). In the National Football League, an average of .41 concussions occur per game, with 69% to 92% of athletes returning to practice within 7 days postinjury (Pellman et al., 2004).

Within military settings, some 22.8% of deployed servicemen and women screen positive for a possible mTBI (Iverson et al., 2009). Presenting an ominous trajectory, the prevalence of head trauma has increased among U. S. military personnel throughout the previous decade, with 77% of military-related brain injuries qualifying as mild (Coronado et al., 2012). Despite the prevalence and public concern surrounding mTBI, past researchers have dismissed its long-term neuropsychological impact as clinically insignificant (Binder, Rohling, & Larrabee, 1997; Frencham, Fox, & Maybery, 2005; Larrabee, Binder, Rohling, & Ploetz, 2013; Rohling et al., 2011; Shretlen & Shapiro, 2003); however, some individuals may remain symptomatic long after the concussive event (Bigler et al., 2013; Pertab, James, & Bigler, 2009), potentially explained by acute neurological impairment that can persist after injury (e.g., Cohen et al., 2007; Holli et al., 2010). Alternatively, some researchers have identified more psychogenic predictors of persistent symptoms (Silverberg & Iverson, 2011).

Persistent symptoms of mTBI remain a contentious issue, with a recent scholarly dialogue closely examining the evidence both for and against their existence (Bigler et al., 2013; Larrabee et al., 2013; Pertab et al., 2009; Rohling et al., 2011). Dating back to the 19th century, scholars have argued between the psychological and physiological etiologies of post-mTBI symptoms (see Binder et al., 1997). Schretlen and Shapiro (2003) designated mTBI as mild head trauma within their review of brain injuries, positing that the trauma described in concussion-related research deals with minor injuries involving no identifiable neurological atrophy. Standard structural neuroimaging usually provides normal results in cases of mTBI (McCrary et al., 2013), but many researchers have explored neurological correlates of these mild injuries. Researchers using functional MRI have produced mixed results, identifying both increases and decreases in blood-oxygen levels among mTBI participants during primarily working memory tasks (Jantzen, 2010). Some structural MRI studies have found group differences in global, axonal, and gray matter atrophy when comparing mTBI patients with control participants (Cohen et al., 2007; Holli et al., 2010). To date, MRI findings on mTBI have found variable results and often merge mild head injury patients with more severe cases

(Shenton et al., 2012). Another structural MRI study reported that intraparenchymal traumatic axonal injuries were highly associated with loss of consciousness in mTBI; however, imaging results did not correlate with long-term impairments in cognitive performance (Lee et al., 2008). These authors posited that Diffusion Tensor Imaging (DTI) may offer future biomarkers predictive of cognitive outcomes. In turn, technological advances in DTI have improved detection of neural abnormalities after minor brain injuries (see Shenton et al., 2012 for review).

Demonstrating a bridge between neurological damage and adverse behavioral change, DTI methods have shown correlations between executive dysfunction and mTBI-related axonal injury in the dorsolateral prefrontal cortex (Lipton et al., 2009). Frontal and temporal white matter damage appears characteristic of mTBI, with both relating to cognitive dysfunction postinjury (Niogi & Mukherjee, 2010). Such neuroimaging abnormalities define a subgroup of minor head injuries historically termed "complicated" mTBI (Williams, Levin, & Eisenberg, 1990) and these acute axonal injuries may explain the long-term impairments described by some patients postinjury (Shenton et al., 2012).

This neurological evidence validates the public concern surrounding mTBI; however, despite the detection of axonal injury, researchers must link neural atrophy to lasting behavioral consequences to understand the full impact of mTBI on everyday life. Linking this atrophy to behavior, neuropsychologists have played an important role in the assessment and management of mTBI (Echemendia et al., 2011; Harmon et al., 2013), with a high sensitivity of neuropsychological tests at detecting the presence of mTBI among athletes (i.e., 71%–88%; Giza et al., 2013). Contributing to mTBI research, many neuropsychological studies have inundated the scientific literature on concussions (Echemendia et al., 2011), exploring cognitive outcomes across memory, attention, executive functions, and many other cognitive domains. In turn, policymakers should understand the abundant neuropsychological research on mTBI to promote informed decision-making in regards to concussion management.

To aid in the formation of evidence-based policy, numerous systematic reviews and meta-analyses have examined the effects of these head injuries (Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005; Belanger, Spiegel, & Vanderploeg, 2010; Belanger & Vanderploeg, 2005; Binder et al., 1997; Broglio & Puetz, 2008; Dougan, Horswill, & Geffen, 2013; Frencham et al., 2005; Pertab et al., 2009; Rohling et al., 2011; Shretlen & Shapiro, 2003; Zakzanis, Leach, & Kaplan, 1999); however, the plethora of reviews likely overwhelms policymakers, having to synthesize and understand sometimes disparate conclusions based, in part, on the same set of studies. The overabundance of meta-analyses likely derived from three evolving features of the research on mTBI. First, (a) preliminary meta-analyses tackled only a handful of existing studies at the time of their publication (Binder et al., 1997; Zakzanis et al., 1999), providing an informative foundation, but also requiring a timely update. Sequentially, (b) studies on mTBI increased rapidly in the previous decade, with updated meta-analyses focusing on more general (Belanger et al., 2005; Frencham et al., 2005; Shretlen & Shapiro, 2003) and specifically athletic samples (Belanger & Vanderploeg, 2005; Broglio & Puetz, 2008; Dougan et al., 2013). And lastly, (c) more recent researchers have sought to replicate past meta-analytic findings by reanalyzing

the same samples of studies as earlier quantitative reviews (Pertab et al., 2009; Rohling et al., 2011). In addition, one unique and recent meta-analysis explored solely the cognitive outcomes of multiple mTBI (Belanger et al., 2010), setting it apart from past reviews.

Considering the mere number of extant meta-analyses, a systematic review of reviews stands as the next logical step in simplifying and synthesizing the conclusions presented by past meta-analytic researchers (Smith, Devane, Begley, & Clarke, 2011). The current review aimed to synthesize the existing reviews in both a communicative and meaningful way by following three aims: (a) to appraise past systematic reviews on neuropsychological outcomes of mTBI; (b) to identify the overall cognitive effect of mTBI and possible variables (e.g., cognitive domain, time since injury) moderating this effect; and (c) to qualitatively synthesize past meta-analytical findings to inform future mTBI-related policy and research.

## Method

### Literature Search

The systematic literature search occurred in December 2012, involving online searches of the following databases with search limits in parentheses: CINAHL (English language meta-analyses and systematic reviews), Cochrane Database of Systematic Reviews (Cochrane reviews), Database of Abstracts of Reviews of Effects, MedLine (English language meta-analyses and reviews), PsycArticles (meta-analyses and systematic reviews), and PsycInfo (English-language meta-analyses and systematic reviews).

Neurotrauma-related search terms included mTBI, concussion, mild traumatic brain injury, mild brain injury, mild head injury, and minor head injury (Belanger et al., 2005); outcome-related search terms included neuropsychology, neuropsychological, assessment, cognitive, cognition (Frencham et al., 2005); and method-related search terms included meta-analysis and systematic review (Montori, Wilczynski, Morgan, & Haynes, 2005; Wilczynski & Haynes, 2007). All retrieved results were screened twice to ensure no study went overlooked (Edwards et al., 2002). In addition to the electronic search method, manual searches of reference lists from peer-reviewed journals continued throughout the data extraction and manuscript preparation process, procuring additional articles included within this review (see Figure 1, for a flow diagram of the systematic review process). One dissertation identified through the electronic search (i.e., Chaney, 2001) could not be obtained for review.

Prior to the literature search process, the authors established specific inclusion criteria for eligible review articles. For inclusion in the systematic review of reviews, articles needed to (a) report a systematic literature review and/or meta-analysis; (b) examine neuropsychological and cognitive outcomes related to mTBI or concussion in any population (i.e., athletic, military, general, etc.); (c) review solely observational research and not experimental interventions for mTBI (e.g., pharmacotherapy, cognitive training); (d) include only studies involving late adolescents or adults (as pediatric brain injuries involve distinct cognitive sequelae; Borg et al., 2004; Carroll et al., 2004); (e) be published in either a peer-reviewed journal or academic book; and (f) be written in the English language.

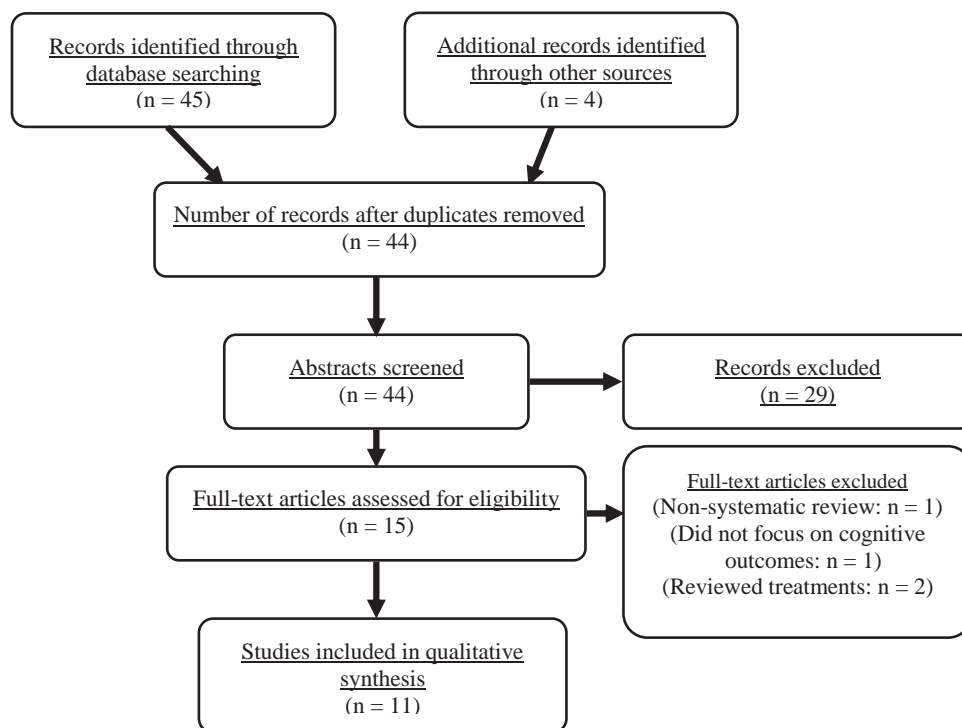


Figure 1. Flowchart of the systematic review.

## Data Extraction

Two independent reviewers systematically extracted information from each quantitative review following a common data collection instrument established specifically for this study. The extracted study characteristics included qualitative summaries of study aims, search strategies, inclusion criteria, and moderator variables. The extracted quantitative variables included year of publication, number of included studies ( $k$ ), sample size with and without concussion (N summed across included studies), average age, percent male, and effect sizes. In the interest of parsimony, not all effect sizes were extracted from each meta-analysis, but just those relevant for the synthesis of conclusions across meta-analyses. All effect sizes were recoded so that a positive value indicated worse performance by the mTBI group.

In addition to these variables, the AMSTAR instrument provided an empirical assessment of systematic review quality, with possible values ranging from 0 to 11 and higher scores indicating greater quality (Shea et al., 2009). The AMSTAR scale involves dichotomous scoring (i.e., 0 or 1) of 11 items related to the methodological rigor of systematic reviews and meta-analyses (e.g., comprehensive search strategy, publication bias assessment). All extracted review information and quality rankings were compared to ensure interrater reliability. The independent reviewers reached 100% correspondence between effect size data points. For the AMSTAR, initial correspondence was 87%; however, discussion over discrepancies ultimately yielded 100% consensus regarding the extracted data.

## Data Synthesis

As each review samples studies from the extant literature, several studies were included in multiple reviews, which likely biases statistical conclusions made by any meta-review (Smith et al., 2011). Consequently, the data synthesis for this systematic review of reviews remained purely qualitative as no formal statistical tests evaluated the quantitative influence of extracted moderators. Conclusions based on moderator variables from the included reviews are detailed extensively in the Results section of this article. As mixed-mechanism and sports-related mTBI have been distinguished from one another by past researchers (e.g., Belanger et al., 2005; Belanger & Vanderploeg, 2005), the outcomes of athletic and general samples are discussed separately under each applicable moderator subsection in the Results portion of this manuscript.

Statistical methods varied across reviews, with some using metaregression (e.g., Broglio & Puetz, 2008; Dougan et al., 2013) and others categorizing effects based on moderators and testing significance for each estimate (e.g., Belanger et al., 2005; Belanger & Vanderploeg, 2005). Conclusions drawn from each meta-analysis were considered and integrated into conclusions independent of the statistical methods used. Meta-analyses varied in their use of fixed and random effects models, which impacted their quality ratings (i.e., fixed effects models received lower scores, Shea et al., 2009). In turn, review quality was considered in the qualitative synthesis and interpretation of moderator variables involving disparate conclusions across meta-analyses.

The majority of studies reported a common effect size ( $d$ , Cohen, 1988), which summarized the mean group difference divided by the pooled sample variance. However, two reviews

(Broglio & Puetz, 2008; Frencham et al., 2005) used an alternative effect size calculation ( $g$ , Hedges, 1981), which produced similar estimates, but used the estimated pooled population variance as the denominator. As well, most of the reviews including  $g$  in their models incorporated a sample-size bias-correction into their effect size formula (Broglio & Puetz, 2008; Frencham et al., 2005; Pertab et al., 2009). Two meta-analyses reported both  $d$  and  $g$  as effect size estimates (Binder et al., 1997; Pertab et al., 2009). For information on the calculation and interpretation of effect sizes, see Durlak (2009).

For the overall extracted effect sizes, the  $U_I/2$  statistic provided additional information regarding the percentage of mTBI participants scoring below the control distribution (Cohen, 1988). Each effect size compares two groups (e.g., mTBI vs. control participants) and has a corresponding  $U_I$  value representing the full percentage of nonoverlap between the distributions for each group. When halved, the resulting  $U_I/2$  value represents the percent of the lower-mean distribution (e.g., the mTBI group) that falls below the higher-mean distribution (e.g., the control group). As recent authors have shown inaccuracy of the traditional  $U_I$  values at quantifying the percentage of nonoverlap (Grice & Barrett, 2013), a supplemental statistic hereafter called  $U_G$  will provide the accurate value for percentage overlap reported alongside the traditional  $U_I$  value.

## Results

The systematic review process yielded 11 meta-analyses included in the following qualitative synthesis (no systematic reviews met inclusion criteria). Table 1 summarizes the aims, procedures, and moderators of the included meta-analyses. The meta-analyses varied in the number of studies included, ranging from eight to 78 studies due largely to different years of publication and diverse inclusion criteria (e.g., sports-related only vs. mixed-mechanism mTBI). Figure 2 schematically demonstrates the number of studies included in each meta-analysis along with overlap in study inclusion across meta-analyses. The sample size (N) of mTBI (range: 264–3,801) and control participants (range: 176–5,631) fluctuated across quantitative reviews. Among the limited studies reporting demographics of their samples (i.e., Broglio & Puetz, 2008; Frencham et al., 2005; Rohling et al., 2011; Zakzanis et al., 1999), mean reported age (range: 19–35) and percent of male participants (range: 64–92.9) differed considerably across reviews. Notably, the only sports-related mTBI meta-analysis reporting sample demographics involved the youngest and most male sample (Broglio & Puetz, 2008). Quality ratings (i.e., AMSTAR scores) ranged significantly across meta-analyses (range: 2–9) and produced a fairly low mean of 4.63 ( $s = \pm 2.25$ ) on a scale of 11 possible quality points. AMSTAR appeared to improve across time, with the highest scores occurring within the last 5 years (Broglio & Puetz, 2008; Dougan et al., 2013); however, two recent meta-analytic replications did not simulate the literature search strategy of the replicated reviews, which strongly impacted their scores (Pertab et al., 2009; Rohling et al., 2011).

A few consistent methodological issues reduced the overall quality of most quantitative reviews. Among included meta-analyses, none listed both included and excluded studies, only one assessed study quality and integrated it into conclusions (Broglio & Puetz, 2008), only three reported using a random effects model

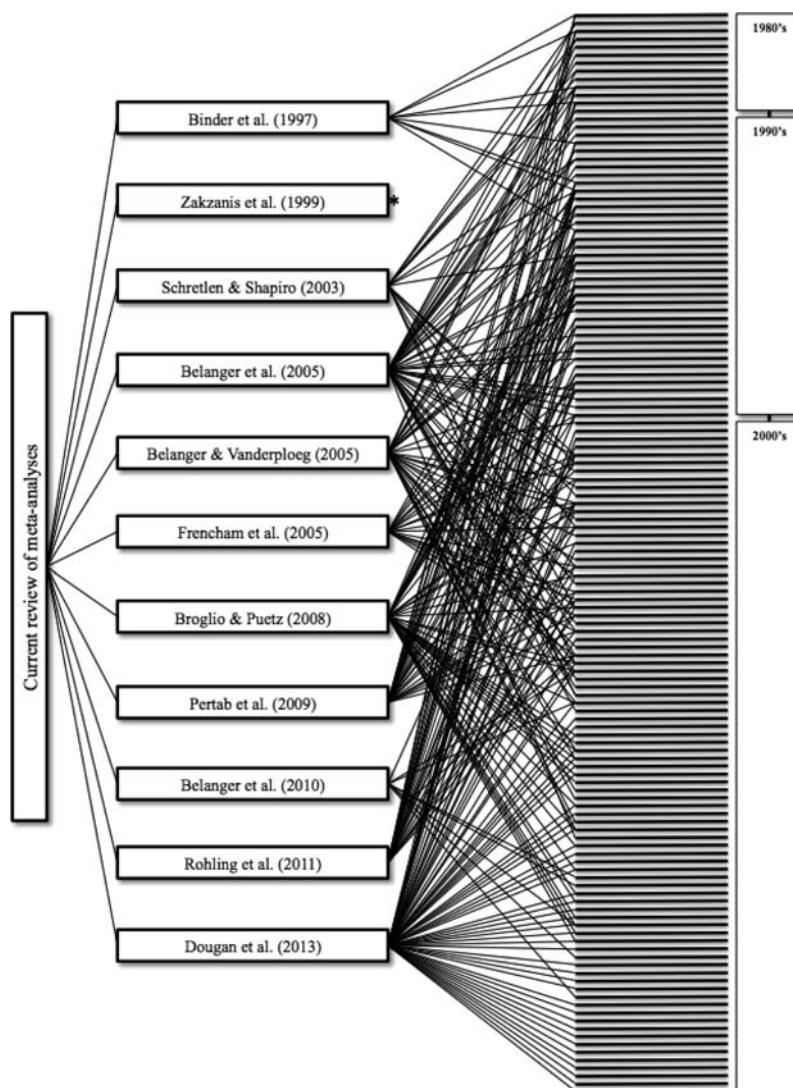
Table 1  
Summary of Systematic Reviews on Neuropsychological Outcomes of mTBI

| Author                 | Year | Aim  | Search strategy   | Search filters  | Keywords listed | Inclusion criteria   | Moderator variables   |
|------------------------|------|--|-------------------|---|-----------------|--|---|
| Binder et al.          | 1997 | To assess cognitive outcomes after mTBI and estimate chronic impairment prevalence   | MedLine           | Published between 1986 and 1994   | No              | (a) Participants had mTBI history, (b) enough info to calculate ES, (c) less than 50% attrition, (d) only mild TBIs included, and (e) only adult participants  | Cognitive domain, mTBI severity (also explored prevalence and predictive value of neuropsychological tests)   |
| Zakzanis et al.        | 1999 | To expand from Binder et al. by examining effect sizes for specific tests            | MedLine, PsycInfo | Published from 1980 to 1997 for manual search                             | Yes             | (a) Involve a healthy control group, (b) enough info for ES calculation, and (c) mTBI diagnosis through Glasgow Coma Scale (13–15), posttraumatic amnesia < 24 hr, loss of consciousness < 20 min, and/or normal imaging                       | Cognitive domain, Specific neuropsychological tests   |
| Schretlen & Shapiro    | 2003 | To estimate the size of effects of mild head injury and TBI on cognitive functioning | Medline, PsycInfo | Published on or before February 2003                                      | No              | (a) English language, (b) involve adult participants, (c) use control group comparison, (d) enough info for ES calculation, and (e) enough info to determine TBI severity  | Time since injury/Recovery rate, Control vs. other injury comparison, TBI severity, Recovery rate, ES formula   |
| Belanger & Vanderploeg | 2005 | To examine the effects of sports-related mTBI on cognition                           | PubMed, PsycInfo  | English language, Human subjects, Published from 1970 to Aug 2004         | Yes             | (a) Participants had sports-related mTBI, (b) standard criteria or professional diagnosis, (c) between or within controlled design, (d) use cognitive outcomes, (e) enough info to calculate ES, and (f) adult or adolescent participants      | Cognitive domain, Time since injury, Assessment method, Control group vs. self-control study design, Participant selection criteria, Previous mTBI, Serial assessment |
| Belanger et al.        | 2005 | To assess how exposure to head injury in sports impacts cognition                    | PubMed, PsycInfo  | English language, Human participants, Published between 1970 and Mar 2004 | Yes             | (a) Participants in head-injury risk sports and (b) use clinically-validated or experimental cognitive measures as outcomes  | Cognitive domain  |
| Belanger et al.        | 2005 | To identify the effects of mTBI on cognition   | PubMed, PsycInfo  | English language, Human participants, Published between 1970 and Mar 2004 | Yes             | (a) Participants seeking medical attention for non-sports-related mTBI, (b) use control group comparison, (c) separate TBI severity, (d) involve cognitive outcomes, (e) enough info to calculate ES, and (f) adult or adolescent participants | Cognitive domain, Time since injury, Participant selection context, Presence vs. absence of validity testing  |

(table continues)

Table 1 (continued)

| Author          | Year | Aim   | Search strategy   | Search filters  | Keywords listed | Inclusion criteria  | Moderator variables   |
|-----------------|------|---|---|---|-----------------|---|---|
| Frencham et al. | 2005 | To assess cognitive outcomes after mTBI across domains along with the influence of stage of recovery  | PsycInfo, Web of Science for studies citing Binder et al. | Not Reported  | Yes             | (a) Published in an English-language journal from 1995 to 2003, (b) used control group comparison, (c) not analyzed in a previous meta-analysis, (d) adult or adolescent participants, (e) separated by TBI severity, (f) included participants regardless of present symptoms, (g) Glasgow scale above 13, (h) involved head impact injuries, and (i) had less than 50% attrition        | Cognitive domain, Time since injury   |
| Broglio & Puetz | 2008 | To quantify the effect of sports-related mTBI on cognition, symptoms and postural control within 14 days postinjury   | PubMed, PsycInfo  | English language, published between Jan 1970 to Jun 2006              | Yes             | (a) Involve athletes with sport-related mTBI, (b) include cognition, symptoms, and/or postural control as outcomes, (c) either self-control or control group, (d) involve post-mTBI assessment by 14 days postinjury, and (e) enough info to calculate ES   | Time since injury, Assessment technique, Control group vs. self-control study design, Number of post-mTBI assessments   |
| Pertab et al.   | 2009 | To reanalyze past meta-analytic findings by Binder et al. and Frencham et al. using different moderators  | Studies cited by Binder et al. and Frencham et al.        | N/A   | N/A             | (a) Data not drawn from convenience sampling, (b) used standardized tests, and (c) enough info to calculate ES  | Time since injury, Assessment tool, Injury mechanism, Diagnostic criteria, Symptomatic vs. nonsymptomatic patient comparisons                                       |
| Belanger et al. | 2010 | To examine the cognitive impact of multiple mTBI  | PubMed, PsycInfo, MedLine                                 | English language, Human participants, Published from 1970 to May 2009 | Yes             | (a) Include only mTBI participants, (b) separate TBI severity, (c) compare multiple mTBI with single mTBI participants, (d) use cognitive outcomes, (e) enough info to calculate ES, and (f) adult or adolescent participants   | Cognitive domain  |
| Rohling et al.  | 2011 | To reanalyze the effect sizes of Binder et al. and Frencham et al. using a random effects model   | Studies cited by Binder et al. and Frencham et al.        | N/A   | N/A             | Same as Binder et al.   | Cognitive domain, Time since injury   |
| Dougan et al.   | 2013 | To evaluate the effect of athlete characteristics on sports-related mTBI outcomes after controlling for known moderators (i.e., time since injury, comparison group, repeated assessment) | PubMed, PsycInfo, MedLine                                 | Papers published from Jan 1970 to Aug 2011                            | Yes             | (a) Published empirical research in an English-language journal, (b) adolescent or adult athlete participants with age or competitive level reported, (c) diagnosed sports-related mTBI, (d) include cognition, symptoms, or postural control as an outcome, (e) postinjury outcome with control group or self-control comparison, and (f) enough info to calculate ES for the mTBI group | Time since injury, Control group vs. self-control study design, Number of postinjury assessments, Age, Years of education, Sex, Level of competition, Sports played |



*Figure 2.* This diagram shows a schematic representation of study inclusion and overlap across meta-analyses. Black lines on the right represent 131 studies included across the 11 meta-analyses (in the center). Three meta-analyses included studies involving sports-related mTBI only (Belanger & Vanderploeg, 2005; Broglio & Puetz, 2008; Dougan et al., 2013). Included in the online supplemental materials, Appendix A includes the references for all 131 studies. \*Zakzanis et al. (1999) did not provide a list of studies included specifically in their mTBI meta-analysis, but instead listed studies included in multiple meta-analyses within their full text.

(Broglio & Puetz, 2008; Dougan et al., 2013; Rohling et al., 2011), only three reported duplicate study selection and extraction (Belanger et al., 2005; Broglio & Puetz, 2008; Dougan et al., 2013), only four assessed the likelihood of publication bias (Belanger et al., 2005; Broglio & Puetz, 2008; Dougan et al., 2013; Zakzanis et al., 1999), and only five reported the status of publication (e.g., published articles, gray literature) as an inclusion/exclusion criteria (Belanger et al., 2005, 2010; Belanger & Vanderploeg, 2005; Frencham et al., 2005; Dougan et al., 2013). In addition to weaknesses, some strengths remained consistent across past meta-analyses, with all reviews reporting a priori designs, all but two reviews (Rohling et al., 2011; Zakzanis et al., 1999) listing the characteristics of included studies, and all but four reviews

(Binder et al., 1997; Frencham et al., 2005; Pertab et al., 2009; Rohling et al., 2011) performing comprehensive literature searches.

Two meta-analyses (Pertab et al., 2009; Rohling et al., 2011) were replications of past meta-analyses (Binder et al., 1997; Frencham et al., 2005) and one meta-analysis (Belanger et al., 2010) focused on multiple mTBI compared with single mTBI as opposed to noninjured controls. Belanger and Vanderploeg (2005) reported two meta-analyses on sports-related mTBI, one related to standard post-mTBI assessments and the other assessed exposure to mTBI through sports involvement (e.g., heading frequency in soccer). Among the excluded studies, one involved a nonsystematic review (Binder, 1986), one focused on methodological quality rather than

cognitive outcomes (Comper, Hutchison, Magrys, Mainwaring, & Richards, 2010), and two summarized experimental mTBI treatments (Comper, Bisschop, Carnide, & Tricco, 2005; Snell, Surgenor, Hay-Smith, & Siegert, 2009).

Table 2 summarizes quantitative study information (e.g., study quality, sample size) as well as reported overall effect size estimates for each meta-analysis and their associated  $U_I/2$  and  $U_G/2$  statistics. The overall effect sizes across meta-analyses ranged from  $g = .07$  (Binder et al., 1997) to  $d = .61$  (Zakzanis et al., 1999) for mixed-mechanism mTBI and from  $d = .40$  (Dougan et al., 2013) to  $g = .81$  (Broglia & Puetz, 2008) for sports-related mTBI. The effects reported by each study present a consistently adverse impact of mTBI on cognition, but each overall estimate derives from many designs (e.g., self vs. control group comparisons, diverse times since injury, etc.). Many meta-analyses derived this estimate by averaging across all postinjury epochs (i.e., acute, postacute, and multiple follow-ups; Belanger et al., 2005, 2010; Belanger & Vanderploeg, 2005; Dougan et al., 2013; Frencham et al., 2005; Pertab et al., 2009; Rohling et al., 2011; Schretlen & Shapiro, 2003; Zakzanis et al., 1999), although others included only acute (i.e., within 14 days of injury; Broglia & Puetz, 2008) or postacute effect sizes in this estimate (i.e., greater than 90 days postinjury; Binder et al., 1997). As many confounding variables impact the overall effect size estimates, the following subsections clarify the moderating influence of various design parameters on the cognitive effects of mTBI.

## Cognitive Domain

Most domains (e.g., executive functions, delayed memory, visuospacial skills, etc.) show staggering variability in effects, with a significant range in effect sizes reported across studies. Although an early meta-analysis concluded that mTBI represented frontal-executive pathology (Zakzanis et al., 1999), more recent meta-analyses have found minimal effects in executive domains (Belanger et al., 2005; Belanger & Vanderploeg, 2005; Rohling et al., 2011). Multiple meta-analyses have incorporated cognitive domain as a moderating variable (Belanger et al., 2005, 2010; Binder et al., 1997; Belanger & Vanderploeg, 2005; Frencham et al., 2005; Rohling et al., 2011; Zakzanis et al., 1999); however, the extracted effect sizes appear surprisingly heterogeneous across reviews (see Table 3 for a summary of effect sizes by cognitive domains). Within the reviewed meta-analyses, different authors may have categorized the same neuropsychological tests into distinct cognitive domains, as shown by a reanalysis of past meta-analytic results assessing test type (e.g., Trails B, Story Memory, etc.) as the moderating variable (Pertab et al., 2009). These researchers identified distinct effect sizes of verbal paired memory, story memory, list memory, and figure memory tests ( $d = .81, .10, .00$ , and  $-.10$ , respectively). The sensitivity of neuropsychological tests in mTBI shows great variability, even within cognitive domains (Zakzanis et al., 1999). In turn, collapsing by more general constructs (e.g., memory) rather than more specific ones (e.g., verbal memory, visual memory, etc.) may have influenced the reported effect sizes across meta-analyses.

Table 2

*Extracted Review Variables, Study Quality Ratings (AMSTAR) and Overall Effect Sizes of mTBI on Neuropsychological Functioning*

| Author                           | Year | (k) | mTBI (N)                   | Control (N) | Mean age | Percent male | AMSTAR* | Effect size                 | $U_I/2^{**}$ | $U_G/2^{**}$ |
|----------------------------------|------|-----|----------------------------|-------------|----------|--------------|---------|-----------------------------|--------------|--------------|
| Binder et al. <sup>#</sup>       | 1997 | 8   | 314                        | 308         |          |              | 2       | $d = .12$<br>$g = .07$      | 3.85<br>3.85 | 2.00<br>2.00 |
| Zakzanis et al.                  | 1999 | 12  | 952                        | 495         | 35       | 64           | 3       | $d = .61^{\text{**}}$       | 19.1         | 11.79        |
| Schretlen & Shapiro <sup>§</sup> | 2003 | 15  | 742                        | 545         |          |              | 4       | $d = .24$                   | 7.35         | 3.99         |
| Belanger & Vanderploeg           | 2005 | 21  | 790                        | 2,014       |          |              | 5       | $d = .49$                   | 16.50        | 9.87         |
|                                  |      |     | 264 <sup>###</sup>         | 176         |          |              |         | $d = .31, d = .71^{\wedge}$ |              |              |
| Belanger et al.                  | 2005 | 39  | 1,463                      | 1,191       |          |              | 7       | $d = .54$                   | 16.50        | 9.87         |
| Frencham et al.                  | 2005 | 17  | 634                        | 485         | 28.46    | 66.27        | 4       | $g = .32^{\text{^^}}$       | 10.65        | 5.96         |
| Broglia & Puetz                  | 2008 | 39  | 4,145 <sup>+</sup>         |             | 19.0     | 92.9         | 9       | $g = .81^{\text{^^}}$       | 23.70        | 15.54        |
| Pertab et al. <sup>#</sup>       | 2009 | 18  | 765                        | 583         |          |              | 3       | $d = .45^{\#}$              | 16.50        | 9.87         |
|                                  |      |     |                            |             |          |              |         | $g = .31$                   |              |              |
| Belanger et al.                  | 2010 | 8   | 614 with 2+,<br>926 with 1 |             |          |              | 5       | $d = .06$                   | 3.85         | 2.00         |
| Rohling et al.                   | 2011 | 25  | 2,834                      | 2,057       | 25.5     | 73.85        | 2       | $d = .28$                   | 10.65        | 5.96         |
| Dougan et al.                    | 2013 | 78  | 3,801                      | 5,631       |          |              | 8       | $d = .40$                   | 13.7         | 7.93         |

*Note.* All positive effect sizes denote worse performance resulting from mTBI. \* AMSTAR study quality ratings ranged from 0 to 11. \*\* As Cohen (1988) and Grice & Barrett, (2013) only published  $U_I$  and  $U_G$ , respectively, values for tenth-sized increment increases in  $d$ , the  $U_I$  and  $U_G$  values used in the  $U_I/2$  and  $U_G/2$  calculations represent percent overlap for each effect size rounded to the nearest tenth (e.g., the  $U_G$  assigned to .06 corresponds to the percent nonoverlap when  $d = .10$ ). <sup>#</sup> Binder et al. (1997) and Pertab et al. (2009) reported two effect size statistics: Cohen's  $d$  and Hedges'  $g$ . Although Pertab et al. used a sample-size bias-correction for  $g$ , Binder et al. did not correct for sample size. <sup>###</sup> Represents participants "exposed" to mTBI due to frequent sports-related head contact (e.g., heading in soccer). <sup>^</sup> Exposure meta-analysis produced two effect sizes, based on unexposed control comparison and exposure-cognition correlations, respectively. <sup>§</sup> Meta-analysis involved both mTBI and moderate and severe TBI studies, but  $k$ ,  $N$ s, and  $d$  values represent only mTBI-related data. <sup>+</sup>  $N$  not divided by mTBI and control group, representative of overall sample size. <sup>^^</sup> Meta-analysis did not report overall effect size, so  $d$  represents an unweighted average across cognitive domains. <sup>^^</sup> Broglia & Puetz and Frencham et al. recruited only a sample-size bias-corrected Hedges'  $g$  for effect size calculation. Although both  $d$  and  $g$  provide very similar values, the corresponding  $U$  statistics were originally calculated based on  $d$ . In turn, the percent overlap values reported above may not be fully accurate for their respective effect sizes. Note also that the overall effect size estimate for Broglia & Puetz derives from initial assessments only within 14 days of injury, explaining its greater magnitude than the effect sizes of other studies.



Table 3  
Effect Sizes by Cognitive Domain

| Authors                | Year | Population            | Global | Orient. | Attn. | WM  | EF   | Fluency | Mem.                 | Delayed mem. | VS skills | Verbal | PS  | Motor |
|------------------------|------|-----------------------|--------|---------|-------|-----|------|---------|----------------------|--------------|-----------|--------|-----|-------|
| Binder et al.*         | 1997 | mTBI                  | .11    |         | .20   |     | -.08 |         | .19                  | .13          |           | -.09   |     | .03   |
| Zakzanis et al.        | 1999 | mTBI                  | .47    |         | .63   |     | .72  |         | .69                  | .71          |           | .62    |     | .44   |
| Belanger & Vanderploeg | 2005 | Sports-related mTBI   | .81    | .27     | .02   |     | -.11 |         | .78                  | .60          |           |        |     |       |
|                        |      | mTBI-exposed athletes | .42    |         | .31   |     | .54  |         | .22                  | .47          | -.16      | .57    |     | .37   |
| Belanger et al.        | 2005 | mTBI                  | .24    |         | .47   |     | .21  | .77     | .35                  | .69          | .57       | .54    |     | .16   |
| Frencham et al.#       | 2005 | mTBI                  |        |         |       | .25 | .30  |         | .30                  |              | -.25      | -.04   | .47 | .40   |
| Belanger et al.        | 2010 | Multiple mTBI         |        |         | .05   |     | .24  | -.09    | .13                  | .16          | .17       |        |     | .10   |
| Rohling et al.         | 2011 | mTBI                  |        |         |       | .33 | .21  |         | .35/.31 <sup>+</sup> |              | .16       | .17    | .15 |       |

Note. All positive effect sizes denote worse performance resulting from mTBI. Orient. = Orientation; Attn. = Attention; WM = Working Memory; EF = Executive Functions; Mem. = Memory; VS = Visuospatial; PS = Processing Speed. Cognitive domains varied across meta-analyses, with some collapsed in the current review. Attention/Concentration, Working Memory/Attention, Cognitive Flexibility/Abstraction, Memory Acquisition, Delayed Recall, Perceptual Organization/Reasoning, Verbal Comprehension/Skills and Language, Global Cognitive Ability and Performance Skills, and Manual Dexterity were subsumed by Attention, Working Memory, Executive Functions, Memory, Delayed Memory, Visuospatial Skills, Verbal, Global, and Motor, respectively.

\* Binder et al. (1997) reported two effect size statistics. Only Cohen's  $d$  is reported in the current table for clarity and improved comparability with effect sizes from other studies, as the majority of studies reported solely  $d$  statistics. # Frencham et al. recruited a sample-size bias-corrected Hedges'  $g$  for effect size calculation while all other effect sizes represent Cohen's  $d$ . + These values represent verbal/visual memory as reported by Rohling et al.

The highest quality meta-analysis assessing cognitive domain focused on mixed-mechanism mTBI (Belanger et al., 2005), finding the highest effects for fluency ( $d = .77$ ) and delayed memory ( $d = .69$ ). Interestingly, these researchers reported small effects for both global abilities ( $d = .24$ ) and memory ( $d = .35$ ), whereas the only sports-related meta-analysis assessing cognitive domain found much larger effects (i.e., global abilities:  $d = .81$ ; memory:  $d = .78$ ; Belanger & Vanderploeg, 2005). Combined, these meta-analyses stand as the most representative of the existing research to date, as more recent reviews examining cognitive domain have focused on solely multiple mTBI (Belanger et al., 2010) or replicated past meta-analyses without an updated literature review (Rohling et al., 2011).

### Cumulative Effects

Studies excluding participants with prior head injury have presented much smaller effects ( $d = .11$ ) than those with no such criterion ( $d = .65$ ; Belanger & Vanderploeg, 2005). In turn, the cumulative effects of mTBI may present more worrisome cognitive outcomes than a single injury; however, the results appear mixed. The overall effect of multiple mTBI compared with single mTBI remains remarkably small ( $d = .06$ ), demonstrating a limited cumulative impact of multiple minor head injuries (Belanger et al., 2010). However, Belanger and Vanderploeg (2005) conducted an exposure-based meta-analysis with studies on cognitive performance among athletes at risk of head injury (e.g., boxing, soccer, etc.). Studies comparing exposed athletes to unexposed control participants produced modest effects ( $d = .31$ ), whereas studies recruiting correlational designs (e.g., heading frequency in soccer by cognition; Webbe & Ochs, 2003) presented much larger effects ( $d = .71$ ). These authors identified a notable impact on executive functions, with an exposure-related effect size ( $d = .54$ ) starkly contrasting the single mTBI-based effect size for this cognitive domain ( $d = -.11$ ). Following this specific cognitive deficit, executive functions appear most sensitive to multiple

mTBI ( $d = .24$ ), standing with delayed memory ( $d = .16$ ) as the only significant effect sizes of cumulative injuries (Belanger et al., 2010). These two meta-analyses (Belanger et al., 2010; Belanger & Vanderploeg, 2005) both presented moderate review quality, but together represent the most recent synthesis of findings on multiple/cumulative mTBI. Many researchers and clinicians would likely conceive of multiple mTBI as chronically detrimental, considering the relation between head injury sports and neurodegeneration (Lehman et al., 2012; McKee et al., 2009); however, few studies have explored the cumulative outcomes of multiple mTBI and researchers have yet to identify a threshold that predicts longstanding neuropsychological impairment (Belanger et al., 2010).

### Time Since Injury

Based on meta-analytic findings, the effects of mixed-mechanism mTBI appear most severe in the acute phases briefly after injury (Schretlen & Shapiro, 2003), but recovery appears to occur rapidly postinjury, with full recovery expected by 90 days (Frencham et al., 2005; Rohling et al., 2011). For sports-related mTBI, the injury results in the same severe acute effects (Broglia & Puetz, 2008; Dougan et al., 2013), but recovery occurs at a much faster rate, with most cognitive domains reaching nonsignificant effects by 7 days postinjury (Belanger & Vanderploeg, 2005). The sports-related meta-analyses involved more recent publications and presented higher review quality, indicating that their findings may more accurately summarize the recovery trajectories of mTBI than the mixed-mechanism research.

Many physiological consequences of mTBI normalize by 2 weeks after the initial injury (Giza & Hovda, 2001; Grindel, 2003), leading Broglia and Puetz (2008) to assess recovery from sports-related mTBI across a 14-day postinjury timeframe. These authors did not find time since injury uniquely predictive of effect size at initial assessment; however, restricted range of time since injury and colinearity of this variable with other predictors in their

metaregression model (i.e., study design and assessment technique) may have diminished its unique significance. Sports-related mTBI may predict faster recovery trajectories, as all cognitive domains (with the exception of delayed memory,  $d = .41$ ) matched controls or exceeded baseline performances beyond 7 days postinjury; however, averaged across domains, a modest effect of mTBI ( $d = .22$ ) remained based on control-group comparisons past these 7 days, whereas within-person designs showed full recovery beyond this timeframe ( $d = -.65$ ; Belanger & Vanderploeg, 2005). Comparatively, a more recent meta-analysis (Dougan et al., 2013) identified a slight increase in effect size from 24 hr postinjury ( $d = .38$ ) to 1–10 days postinjury ( $d = .54$ ), but this trend reversed (i.e.,  $d = .90$  at 24 hr;  $d = .41$  at 1–10 days) when including only effect sizes from more rigorous designs (i.e., those involving both self-control and independent control group comparisons). Considering these inconsistencies, the limited window of up to 14 days postinjury may not allow enough variance to truly encompass the duration of cognitive recovery, as other meta-analysts (Belanger et al., 2005; Frencham et al., 2005) have categorized time since injury as either acute ( $< 90$  days post-mTBI) or postacute ( $\geq 90$  days post-mTBI). This demarcation likely dates back to the inclusion criteria of Binder et al. (1997), as these authors excluded studies involving patients within 90 days of mTBI in order to evaluate long-term cognitive deficits.

Multiple researchers have claimed that average cognitive functioning returns to baseline by 90 days (Frencham et al., 2005; Rohling et al., 2011), although others have identified nonsignificant effect sizes by 30 to 89 days postinjury (Schretlen & Shapiro, 2003). Despite similar values, Frencham et al. (2005) reported the average acute effect size ( $g = .33$ ) as significantly greater than zero, yet the average postacute effect size ( $g = .28$ ) remained nonsignificant due to greater variability in the postacute effects. Treating time since injury continuously, cognitive ability improved with time across the acute phase, but this correlation failed to reach significance in the postacute phase (Frencham et al., 2005). Other researchers on mixed-mechanism mTBI have provided narrower recovery windows rather than the acute/postacute dichotomy (Rohling et al., 2011; Schretlen & Shapiro, 2003), identifying consistent improvement across time. Shortly after injury, recovery appears rapid, but decelerates into the postacute phase as cognition returns to baseline levels (Schretlen & Shapiro, 2003). According to Rohling et al. (2011), this recovery trajectory holds true across all cognitive domains except working memory, which remained slightly impaired ( $d = .19$ ) past 93 days postinjury.

### Persistent Postacute Symptoms

Past researchers have indicated that a subgroup of patients with mTBI may present longstanding impairment (Bigler, 2008; Frencham et al., 2005); however, this symptomatic subsample has remained predominantly unexplored to date (Pertab et al., 2009). The size of this subgroup ranges across studies (Belanger et al., 2005), but one meta-analysis (Frencham, Fox, & Maybery, 2005) recruited a Cohen's  $U_j$  statistic (Cohen, 1988) to quantify the nonoverlap between mTBI and control group distributions, claiming that 21.3% of the mTBI distribution fell below the control distribution for an effect size averaged across all epochs postinjury. However, the  $U_j$  value represents the full nonoverlap across two ideal distributions (both left and right tails), meaning only half

the value (i.e., 10.65% for Frencham et al., 2005) falls below the control distribution (5.96% if using the  $U_G$  statistic). To identify impairment prevalence, Binder et al. (1997) accurately applied the  $U_j/2$  value, finding a 4.6% prevalence of longstanding cognitive impairment among participants with mTBI (2% if using the  $U_G$  statistic). Individual studies tracking long-term outcomes of mTBI have identified 9% of athletes not returning to baseline postconcussion (McCrea et al., 2003) and 10% of a nonathletic group remaining symptomatic at a 1-year follow-up (von Wild, 2008). This subgroup presents a more chronic pattern of symptoms; and, when considered separately from nonsymptomatic participants, they present a more prominent level of neuropsychological impairment (Bigler, 2008).

The variables moderating this subsample remain unexplored to date, but one review explored symptomatic subgroups as a moderating variable (Pertab et al., 2009). Although too few studies examined this variable to allow for a quantitative assessment, these authors identified a handful of studies potentially explaining the durability of post-mTBI symptoms in some participants. This subsample presented a higher likelihood of having a past brain injury, neurological or psychiatric problem, or injury related to a motor vehicle accident. In addition, they were more likely to be female (Ponsford et al., 2000). Past adverse neurological events predict worse outcomes after mTBI, aligning with the more pervasive effects of repeated exposure to head injury on cognitive performance (Belanger & Vanderploeg, 2005).

Some evidence has also associated compensation-seeking and litigation with prolonged symptoms. Belanger et al. (2005) found that most cognitive domains presented significant effect sizes past 90 days, but sample selection context further moderated the heterogeneity in recovery rates. Past researchers have identified potential links between compensation-seeking and persistent symptoms in the postacute phase of mTBI (Kashluba, Paniak, & Casey, 2008), as litigation-based samples increased in symptoms beyond 90 days postinjury and unselected samples presented essentially full recovery within this timeframe; however, these authors found similar long-term symptom profiles in clinic-based patients as well (Belanger et al., 2005). This subsample presents a potential avenue for future research on mTBI; however, some have posited that this symptomatic subgroup derives from statistical error rather than any existing phenomenon (Rohling et al., 2011). Still, proper meta-analytic methods can obscure individual differences in cognitive recovery rates, as generalized conclusions of full recovery for all patients by 3-months postinjury remain conceivably incorrect (Iverson, 2010). Unfortunately, the few meta-analyses attempting to explore or quantify this subgroup remain low in quality and involved outdated and nonrepresentative subsamples of the existing research on mTBI (Binder et al., 1997; Frencham et al., 2005; Pertab et al., 2009).

### Participant Characteristics

A recent and high-quality meta-analysis (i.e., Dougan et al., 2013) specifically assessed the impact of participant-level variables (e.g., gender, athletic competitive level) on neuropsychological outcomes following sports-related mTBI, focusing specifically on these moderators at 1–10 days postinjury among an athletic population. Through an innovative approach, these authors iden-

tified a series of moderators of mTBI outcomes, including gender, age, education, competitive level, and sport affiliation.

Gender moderated neuropsychological outcomes, with female athletes ( $d = .87$ ) presenting much larger effect sizes than male athletes ( $d = .42$ ). As continuous variables in metaregression models, age, and education both predicted post-mTBI neuropsychological outcomes, with increases in each variable protecting against cognitive sequelae. More contextually, competitive level served as an explanatory moderator, with high school competition ( $d = .60$ ) presenting larger effects than both professional ( $d = .43$ ) and collegiate levels ( $d = .41$ ). For sports affiliation, only samples involving American football athletes presented a sufficient number of effect sizes to facilitate interpretation ( $d = .53$ ), as sparse representation of other sports limited the breadth of this moderator.

### Comparison Group

Independent control group comparisons appear to predict larger effect sizes across both general and athletic samples (Belanger & Vanderploeg, 2005; Broglio & Puetz, 2008; Dougan et al., 2013), as within-person control designs may diminish the magnitude of long-term mTBI-related impairment due to practice effects. Broglio and Puetz (2008) did not identify the number of post-mTBI assessments as predictive of effect size, but found reductions in magnitude from first to follow-up assessments. Similarly, Belanger and Vanderploeg (2005) found that single assessments produced effect sizes more than twice as large as those associated with serial assessments. The impact of repeated measurement remains hard to delineate, as time since injury, repeated assessment, and comparison group all interact to affect the cognitive outcomes of mTBI (Dougan et al., 2013). In addition, studies recruiting healthy control groups or self-control comparisons did not yield significantly different effect size estimates than studies comparing the mTBI group to participants with a history of "other" traumatic injuries; however, as expected, mTBI participants present a smaller magnitude of cognitive impairment with a far greater cognitive prognosis than participants with moderate and severe brain injuries (Schretlen & Shapiro, 2003).

### Assessment Technique

With mTBI characterized by subtle cognitive deficits, neuropsychological assessment has presented a low positive predictive value, with very limited accuracy of detecting brain injury after mTBI through abnormal test results (Binder et al., 1997). However, since Binder and colleagues published their early findings, newer tests and computerized administrative techniques have become more prevalent. In turn, the style of neuropsychological assessment recruited by researchers appears to moderate the detected cognitive outcome of sports-related mTBI. Although computerized tests ( $d = .61$ ;  $g = .70$ ) and paper-and-pencil tests ( $d = .51$ ;  $g = .61$ ) produce similar effect sizes (Belanger & Vanderploeg, 2005; Broglio & Puetz, 2008), the standardized assessment of concussion (SAC) technique (McCrea, 2001) tends to produce a much larger overall effect ( $g = 1.49$ ) across studies (Broglio & Puetz, 2008). At initial assessment, the SAC detects larger effects (likely due to the immediacy of its sideline application), but this advantage shifts to paper-and-pencil techniques at follow-up assessments (Broglio & Puetz, 2008).

In addition to neuropsychological assessment, two recent and high-quality meta-analyses explored both symptom reports and postural control as mTBI-related outcomes. Within the acute phases of injury (i.e., ~1–14 days post-mTBI), these two metrics found much higher effect sizes than neuropsychological measures. Postural control resulted in large effects ( $g = 2.56$ ;  $d = 1.10$ ) along with self-report symptoms ( $g = 3.31$ ;  $d = 1.14$ ; Broglio & Puetz, 2008; Dougan et al., 2013). Although beyond the scope of the current review, their clear sensitivity to mTBI supports their utility in a comprehensive mTBI assessment.

### Diagnostic Criteria

Since the earliest studies on the neuropsychological outcomes of mTBI, the criteria for defining mild head trauma has remained inconsistent and nonuniform (Binder et al., 1997). One older meta-analysis requiring fairly strict diagnostic criteria for inclusion reported fairly high effect sizes across cognitive domains (i.e.,  $d = .44$  to  $.72$ ; Zakzanis et al., 1999). Attempting to explore diagnostic criteria as a moderating variable, Pertab, James, and Bigler (2009) identified too much heterogeneity in the selected criteria across studies, ranging from established American Academy of Neurology guidelines (i.e., Kelly et al., 1997) to discerning blows to the head. Consistency in diagnostic criteria by future authors would facilitate the exploration of this moderator by future meta-analysts.

### Discussion

The overall effect of mTBI ranged across meta-analyses (i.e.,  $g = .07$  to  $d = .61$  for mixed-mechanism mTBI and  $d = .40$  to  $g = .81$  for sports-related mTBI); however, specific moderating variables (e.g., cognitive domain, time since injury) accounted for some of this heterogeneity in outcomes. Although cognitive domain served as an informative moderator within each meta-analysis, effect sizes within each domain appeared particularly inconsistent across quantitative reviews, likely deriving from sampling error across meta-analyses (e.g., overly strict or lenient inclusion criteria) or inconsistent operational definitions for each neuropsychological domain (e.g., Belanger & Vanderploeg, 2005, included fluency tests as executive functions, yet Belanger et al., 2005, defined fluency as a separate construct). This result demonstrates a fundamental dearth in the scientific understanding of post-mTBI impairment based on cognitive construct; and in turn, the magnitude of mTBI-related effects within each cognitive domain remains unclear. Considering this issue, executive functions appear specifically unique. The respective effect sizes of this construct appear especially heterogeneous across meta-analyses (i.e.,  $d = -.11$  to  $.72$ ), but these higher-order functions appear most susceptible to multiple mTBI ( $d = .24$ ; Belanger et al., 2010) and second-most susceptible to head injury exposure ( $d = .54$ ; Belanger & Vanderploeg, 2005). In turn, future mTBI research should apply established operational definitions of executive functions (e.g., Miyake et al., 2000) to improve their measurement accuracy when assessing abilities within this complex cognitive domain.

Cognitive domains also differed in their recovery rates postinjury (Belanger et al., 2005); but overall, time since injury presented

a consistent influence on the magnitude of effects, with the long-term cognitive impact of mTBI subsiding in most individuals by 90 days postinjury (Frencham et al., 2005; Rohling et al., 2011; Schretlen & Shapiro, 2003). Others have posited more rapid recovery windows, specifically among athletes (i.e., 7 days, Belanger & Vanderploeg, 2005); however, many meta-analyses on sports-related concussion have been constrained by limited research exploring cognitive outcomes past 7–10 days (e.g., Belanger & Vanderploeg, 2005; Broglio & Puetz, 2008; Dougan et al., 2013), with more research required to predict delayed recovery trajectories among head-injured athletes. Although the average prognosis appears positive, a subgroup of patients with mTBI may remain chronically impaired into the postacute phase (Bigler et al., 2013; Frencham et al., 2005; Pertab et al., 2009), but the size (Belanger et al., 2005) and existence (Larrabee et al., 2013; Rohling et al., 2011; Rohling, Larrabee, & Millis, 2012) of this symptomatic subgroup remains debatable. Focusing on mean performances, meta-analytic methods may hide the few participants presenting persistent symptoms post-mTBI (Iverson, 2010). Further, multiple biomarkers (e.g., DTI, eye tracking) have detected nontransient neurological changes following mTBI (Bigler et al., 2013), evidencing the potential for long-term impairment. However, these persistent symptoms could also derive from preexisting psychological factors (e.g., psychosocial stressors, lower cognitive ability) rather than representing outcomes attributable to the mild head injury itself (Larrabee et al., 2013). As posited by past researchers, many moderating variables also predict the presence of persistent symptoms (e.g., compensation-seeking, Kashluba et al., 2008; more severe neurological damage, Levine et al., 2008), but few studies have examined these symptomatic participants with the needed specificity to fully explain their chronic profiles (Pertab et al., 2009). Interestingly, greater education results in smaller acute effects of mTBI among athletes (Dougan et al., 2013), which may indicate the importance of cognitive reserve for mTBI outcomes (Satz, 1993); however, no review explored education in relation to long-term outcomes.

Chronic symptom profiles remain highly important considering the concerns surrounding the long-term consequences of mTBI among retired athletes (Guskiewicz et al., 2005; McKee et al., 2009). Although most meta-analyses identify fairly rapid cognitive symptom resolution, some underlying and persistent factor must explain the increased risk for dementia among American football players (Lehman et al., 2012) despite normal neurobehavioral presentations. Even in the presence of normal cognitive profiles, underlying neurophysiological dysfunctions can appear (e.g., Pontifex, O'Connor, Broglio, & Hillman, 2009), indicating a compensatory neuromodulation to retain normal cognitive task performances. In turn, the brain may functionally adjust in response to mTBI, producing adaptive systematic changes, perhaps following a cognitive scaffolding commonly associated with normative aging (Park & Reuter-Lorenz, 2009); however, when the retired athletes with multiple mTBI reach an age of typical cognitive decline, underlying normative changes in the brain may induce dementia onset in an already atrophied system. In turn, despite normal neuropsychological presentations, latent pathologies potentially remain, with clinicians likely requiring more sensitive measures to detect ongoing functional deficits.

## Unexplored Moderating Variables

Aside from the moderating variables discussed in past meta-analyses, numerous theoretical variables may influence cognitive outcomes post-mTBI. Future researchers should more closely examine how the mechanisms of mTBI impact cognitive functioning. Both biomechanics and injury etiology may explain some variance in mTBI outcomes (Pertab et al., 2009). Head impact location (Viano, Casson, & Pellman, 2007) and neck strength (Zwahlen, Labler, Trentz, Grätz, & Bachmann, 2007) both influence the neurological outcomes of concussive events. As well, athletic populations may have unique experiences of mild head trauma compared with the general population, considering their physical fitness and desire for return-to-play (Belanger & Vanderploeg, 2005); however, although many meta-analyses have separately explored mixed-mechanism and sports-related mTBI, no existing reviews have quantitatively compared effect sizes derived from athletic and nonathletic samples. Further complicating the issue, most sports-related studies involve predominantly male participants (Comper et al., 2010), although gender clearly impacts cognitive outcomes after mTBI (Dougan et al., 2013).

Among the studies sampled by Rohling et al. (2011), men accounted for 73.4% of participant pools with reported gender makeup. Among sports-related mTBI studies, males compose the majority of most samples (Broglio & Puetz, 2008), as many studies focus on American football alone (Comper et al., 2010). This gender bias in sampling likely results from the higher prevalence of mTBI among males (Cassidy et al., 2004); however, when matched by sport, females present a higher rate of mTBI than the opposite gender (Gessel et al., 2007), which presents the importance of expanding mTBI research across more representative samples. Although not exhaustive, individual studies have presented disparate results in relation to cognitive outcomes of mTBI (e.g., minor female advantages, Moore, Ashman, Cantor, Krinick, & Spielman, 2010; minor male advantages, Colvin et al., 2009; no long-term differences, Tsushima, Lum, & Geling, 2009). One meta-analysis assessed gender as a moderator (Dougan et al., 2013); however, their review involved effect sizes on neuropsychological outcomes at only 1–10 days post-mTBI. In turn, future researchers must examine gender differences past acute recovery phases to further identify person-level predictors of long-term cognitive outcomes.

Although gender and other moderating variables remain unexplored, the interactions between moderators evaluated within this review also appear fairly unclear and especially problematic when interpreting meta-analytic results. As athletic samples consist of predominantly male participants, conclusions surrounding sports-related mTBI remain confounded due to numerous moderating variables potentially affecting the outcomes of each research study, including physical fitness, gender (Dougan et al., 2013), and time since injury (Belanger & Vanderploeg, 2005). As well, past head injuries may impact the neuropsychological outcomes of mTBI (Belanger et al., 2010; Ponsford et al., 2000), with past unreported (Langlois et al., 2006) or unidentified concussions (Mansell et al., 2010) among athletic participants further confounding research findings. Although some researchers have attempted to assess the interactions between moderators (e.g., time since injury by cognitive domain, Belanger & Vanderploeg, 2005; time since injury by sample selection context, Belanger et al., 2005), many interactions

remain fully unexplored (e.g., gender by cognitive domain, education by time since injury), which should guide future empirical and meta-analytic investigations evaluating the cognitive sequelae of mTBI.

### Limitations and Methodological Concerns

In addition to the identified moderating variables, both design and analytical issues may explain disparate findings, as most of the extant meta-analyses present methodological flaws. None of the authors included unpublished or gray literature in their meta-analyses, introducing a publication bias in their reported findings (Laws, 2013). Only three meta-analyses included in this review assessed publication bias (through funnel plots, Broglio & Puetz, 2008; Dougan et al., 2013; indirectly through a fail-safe  $N$ ; Zakzanis et al., 1999), but all three identified a limited impact of this methodological concern. However, the validity of each meta-analysis not assessing publication bias remains threatened by the file-drawer problem (i.e., a positive skew of results due to a publication bias against null result dissemination; Rosenthal, 1979), and the systematic review of reviews methodology may only amplify this bias, suggesting a cautionary interpretation of the reviewed results. As well, the current review did not exclude meta-analyses based on inadequate clinical definitions of mTBI, although the meta-analyses varied in their own inclusion criteria from Glasgow scores (e.g., Frencham et al., 2005; Zakzanis et al., 1999) to professional diagnoses (e.g., Belanger & Vanderploeg, 2005; Dougan et al., 2013) to merely self-report (Belanger et al., 2010). In turn, the conclusions drawn derive from a somewhat heterogeneous sample of mTBI diagnoses, which further limits the current summary of meta-analytic findings.

Other methodological and analytical flaws presented themselves across quantitative reviews. Two meta-analyses represented re-analyses (i.e., Pertab et al., 2009; Rohling et al., 2011) of past reviews without including replicated literature searches. As well, only three meta-analyses used random-effects models in cases of significant heterogeneity (Broglio & Puetz, 2008; Dougan et al., 2013; Rohling et al., 2011). In turn, review quality (i.e., AMSTAR scores) remained fairly low across meta-analyses, potentially biasing their summative findings and conclusions. A few common misses consistently penalized review quality of the included meta-analyses. As no authors listed the excluded studies from their literature review, their readership cannot identify the specific studies unrepresented by their quantitative synthesis, along with their reasons for exclusion. Only one author assessed study quality (Broglio & Puetz, 2008), which largely impacts the interpretation of meta-analytic outcomes.

Although not included in the systematic review, Comper et al. (2010) examined methodological quality of extant empirical studies on the cognitive outcomes of mTBI. These researchers identified significant variability in study quality, an important variable ignored by most meta-analysts when interpreting their synthesized results. Claims regarding cognitive recovery by some meta-analyses (e.g., Schretlen & Shapiro, 2003) have derived predominantly from cross-sectional studies, with a need for more prospective and longitudinal designs to assess the validity of these conclusions (Comper et al., 2010).

Aside from study quality, sampling bias likely impacts the results of more recent quantitative reviews. As mentioned earlier,

two meta-analyses involved preexisting meta-analytical datasets (Pertab et al., 2009; Rohling et al., 2011). As well, only three new meta-analyses (Belanger et al., 2010; Broglio & Puetz, 2008; Dougan et al., 2013) have presented novel findings since 2005 (Belanger et al., 2005; Belanger & Vanderploeg, 2005; Frencham, Fox, & Maybery, 2005) despite a burgeoning body of related studies within that timeframe (Pertab et al., 2009). In turn, numerous studies remain excluded from many meta-analytical findings, resulting from inadequate literature searches or overly restrictive inclusion criteria by some recent meta-analytical authors (e.g., Frencham et al., 2005; Pertab et al., 2009; Rohling et al., 2011).

The most recent meta-analysis provided a highly comprehensive review, likely resolving some of this sampling bias (Dougan et al., 2013); however, they did not reexplore all moderating variables (e.g., cognitive domain) in their review, leaving more room for future meta-analytic updates and replications. As well, more recent studies may have adapted their methods and measurements to improve the detection of mTBI-related impairments, as neurophysiological measures have presented improved detection of long-standing impairment over neuropsychological tests (Broglio, Moore, & Hillman, 2011). Consequentially, a more recent meta-analysis on both psychological and physiological outcomes appears essential to fully update the scientific understanding of mTBI and explore the many moderating variables that remain unidentified to date (Belanger & Vanderploeg, 2005).

Aside from meta-analytic limitations, individual studies remain the most integral component of mTBI research. Comper et al. (2010) explored individual study quality and detailed methods for improving empirical research on mTBI. Meta-analysis fully depends on the quality of empirical studies to derive meaningful conclusions from the literature. Future researchers must report enough information for meta-analysts to calculate and synthesize effects (e.g., participant demographics, descriptive statistics). In particular, means and  $p$  values are not sufficient. As a bare minimum, researchers should report group means and standard deviations, as well as the standard errors of any reported statistics. It is distressingly common in meta-analysis for otherwise informative research to be excluded because the authors do not include enough information for effect sizes to be calculated.

### Future Directions in Neuropsychological Research on mTBI

Although many moderators remain unexplored, mixed-mechanism and sports-related mTBI appear well-represented within the existing research on minor head injury. Many meta-analyses focusing specifically on sports-related injury identified distinct effect size estimates (Broglio & Puetz, 2008; Dougan et al., 2013) and recovery rates (Belanger & Vanderploeg, 2005) when compared with reviews involving more general samples (Frencham et al., 2005; Rohling et al., 2011). In turn, the mechanism of injury remains essential to understanding neuropsychological outcomes, with blast-related mTBI recently becoming the characteristic head injury of military populations (Elder & Cristian, 2009). Aside from traditional blunt force trauma, blast-related TBI involves the impulse of force from an explosion through the head, occurring even when the soldier wears a protective helmet (French, Spector, Stiers, & Kane, 2010). The physical and psychological consequences of this style of brain injury remain rela-

tively unexplored, although blast-related injuries have become the most frequent cause of trauma in the Iraq and Afghanistan wars (Okie, 2005). In turn, blast-related mTBI remains an important area for clinical neuropsychological science, as future researchers further examine the neurobehavioral consequences of mild brain injury.

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