A Systematic Review of Meta-Analyses on the Cognitive Sequelae of mild Traumatic Brain Injury and an Empirical Study on Executive Functions and Intra-Individual Variability following Concussion

by

Justin Elliott Karr
Bachelor of Science, Western Oregon University, 2011

A Thesis Submitted in Partial Fulfillment
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Supervisory Committee

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Mauricio A. Garcia-Barrera, Department of Psychology
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Scott M. Hofer, Department of Psychology
Departmental Member

Abstract

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Mild Traumatic Brain Injury (mTBI), often called concussion, has become a growing public health concern, prevalent in both athletic and military settings. In response, many researchers have explored cognitive outcomes post-mTBI, with a plethora of meta-analyses summarizing these findings; however, these meta-analyses examine solely mean performances on cognitive tasks, ignoring intra-individual variability (IIV) in cognitive performance that may elucidate neuropsychological impairment following mTBI. The current thesis involved two studies, responding to both the growing meta-analytic research and limited IIV findings.

Study 1: Many meta-analyses have amalgamated individual study results on post-mTBI neuropsychological outcomes. With the abundance of meta-analyses, a systematic review of meta-analyses stands as the next logical step. **Method:** A systematic literature search 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 post-injury for most individuals and by seven days post-injury for athletes. Greater age/education and male gender produced smaller effects sizes, while high school athletes suffered the largest deficits post-mTBI. Control-group comparisons yielded larger effects than within-person designs, while 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.

Study 2: The long-term outcomes of executive functions and IIV following mTBI are unclear due to inconsistent and limited research, respectively. Further, the relationship between physical activity (PA) and cognitive performance at young adulthood remains almost fully unexplored. In turn, the current study aimed to (a) assess the diagnostic utility of both executive functions and IIV at predicting mTBI history and (b) evaluate the interaction between PA levels and mTBI on both of these cognitive metrics. **Method:** Altogether 138 self-identified athletes (M_{age} = 19.9 ± 1.91 years, 60.8% female, 19.6% 1 mTBI, 18.1% 2+ mTBIs) completed three executive-related cognitive tasks (i.e., N-Back, Go/No-go, Local-Global). Ordinal logistic regression analyses examined the joint effect of person-mean and IIV as predictors of mTBI status. Multi-level models examined mTBI and PA levels as predictors of trial-to-trial changes in performance. **Results:** Only mean response time (RT) for the Local-Global task predicted mTBI status, while no IIV variables reached unique significance. PA levels predicted subtle within-task decreases in RT across Local-Global trials. **Conclusions:** IIV research on mTBI remains limited; however, the preliminary results do not indicate any additional predictive value of IIV

indices above mean performances. For executive functions, shifting appeared most affected, with past researchers identifying post-mTBI impairment in attentional processing. Higher PA levels minutely benefited within-task shifting and mean inhibitory performance, although these finding require cautious interpretation.

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Dedication

I dedicate this thesis to my family – my mother, father, sister and brother...and my cats and dogs too.

Prologue

As described in the abstract, the following thesis consists of two research articles exploring topics related to neuropsychological assessment and mild Traumatic Brain Injury (mTBI, also known as concussion). The first article involves a systematic review of meta-analyses examining the cognitive outcomes of mTBI and moderating variables affecting these outcomes (e.g., cognitive domain, time since injury). The second article consists of an empirical study exploring both executive functions and a phenomenon called intra-individual variability (IIV) following mTBI. IIV refers to variability in trial-to-trial performance (often called inconsistency) or variability across standardized performances on a neuropsychological test battery (often called dispersion). Notably, IIV overlaps with executive functions in the neural substrates believed to elicit each phenomenon, implying that impairment in one may lead to deficits in the other.

The two articles are related to each other as cognitive research studies on mTBI, but prepared as if autonomous articles, introducing some redundancies in reviewed literature and conclusions drawn; however, as combined under one thesis, the articles fulfilled three research aims related to mTBI research: (a) synthesizing the current knowledge surrounding the cognitive sequelae of mTBI, (b) examining cognitive impairment following mTBI through three established components of executive functions (i.e., updating, shifting, and inhibition), and (c) exploring IIV in cognitive performance as a potentially novel indicator of long-term post-mTBI impairment. In scope, the systematic review and empirical study remain summative and exploratory, respectively; with methodological limitations discussed for each article to guide both interpretation and further research.

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

Abstract

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 post-injury for most individuals and by seven days post-injury for athletes. Greater age/education and male gender produced smaller effects sizes, while high school athletes suffered the largest deficits post-mTBI. Control-group comparisons yielded larger effects than within-person designs, while 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

Introduction

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 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 head impact 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, while women's soccer and ice hockey presented disconcertingly high concussion rates (i.e., .41 and .91 per 1000 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 seven days post-injury (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 United States military 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; Shretlen & Shapiro, 2003); however, some individuals may remain symptomatic long after the concussive event (Pertab, James, & Bigler, 2009), potentially explained by acute neurological atrophy that can persists after injury (e.g., Cohen et al., 2007; Holli et al., 2010). However, some researchers have identified more psychogenic predictors of persistent symptoms (Silverberg & Iverson, 2011).

Persistent symptoms of mTBI remain a contentious issue. Dating back to the nineteenth 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 (McCrory et al., 2013), but many researchers have explored neurological correlates of these mild injuries. Researchers using functional magnetic resonance imaging (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 grey matter atrophy when comparing mTBI patients to 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 case (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, both relating to cognitive dysfunction post-injury (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 post-injury (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 & Vanderploeg, 2005; Belanger, Spiegel, & Vanderploeg, 2010; 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, 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 re-analyzing 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 through EBSCOhost 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 (Frenchman et al., 2005); and method-related search terms included meta-analysis and systematic review (Montori, Wilczynski, Morgan, & Haynes, 2005; Wilczynski & Haynes, 2007). No limits were placed on dates of coverage for any databases. The full electronic search details for this protocol in EBSCOhost are listed in Appendix A for the ease of replication. 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. Although the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher et al., 2009) were not developed for systematic reviews of reviews, some of the preferred reporting items apply to the meta-review methodology, with the PRISMA checklist included in Appendix B.

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 aim, search strategy, inclusion criteria, and moderator variables. The extracted quantitative variables included year of publication, number of studies included (*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 instead only the overall effect size and those divided by cognitive domain. All effect sizes were re-coded 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 with 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 inter-rater 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 manuscript. As mixed-mechanism and sports-related mTBI have been distinguished from one another by past researchers (e.g., Belanger & Vanderploeg, 2005; Belanger et al., 2005), distinction between the outcomes of athletic and general samples are distinguished under each applicable moderator subsection in the results.

Statistical methods varied across reviews, with some using meta-regression (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 & Vanderploeg, 2005; Belanger et al., 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_1/2 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_1 value representing the full percentage of non-overlap between the distributions for each group. When halved, the resulting U_1/2 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_1 values at quantifying the percentage of non-overlap (Grice & Barrett, 2013), a supplemental statistic hereafter called U_G will provide the accurate value for percentage overlap reported alongside the traditional U_1 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 8 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: 264-3801) and control participants (range: 176-5631) 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., 2009; 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 = ±2.25) on a scale of 11 possible quality points. AMSTAR appeared to improve across time, with the highest scores occurring within the last five 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 (Broglio & Puetz, 2008; Dougan et al., 2013; Rohling et al., 2009), 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, grey literature) as an inclusion/exclusion criteria (Belanger & Vanderploeg, 2005; Belanger et al., 2005, 2010; 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 to single mTBI as opposed to non-injured controls. Belanger and Vanderploeg (2005) reported two meta-analyses on sports-related mTBI, one related to standard post-mTBI assessments while the other assessed exposure to mTBI through sports involvement (e.g., heading frequency in soccer). Among the excluded studies, one involved a non-systematic 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 $U_1/2$ 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 (Broglio & 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 post-injury epochs (i.e., acute, post-acute, and multiple follow-ups; Dougan et al., 2013; Frencham et al., 2005; Rohling et al., 2011), while others included only acute (i.e., within 14 days of injury; Broglio & Puetz, 2008) or post-acute effect sizes (i.e., greater than 90 days post-injury; Binder et al., 1997). A number of meta-analyses merely averaged the estimated effect sizes of individual studies to produce the reported overall effect (Belanger & Vanderploeg, 2005; Belanger et al., 2005, 2010; Pertab et al., 2009; Schretlen & Shapiro, 2003; Zakzanis et al., 1999). 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, visuopatial skills, etc.) show staggering variability in effects, with a significant range in effect sizes reported across studies. While 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 & Vanderploeg, 2005; Belanger et al., 2005; Rohling et al., 2011). Multiple meta-analyses have incorporated cognitive domain

as a moderating variable (Binder et al., 1997; Belanger et al., 2005; Belanger & Vanderploeg, 2005; Belanger et al., 2010; 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 re-analysis 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). Sensitivity of neuropsychological tests in mTBI show 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.

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 to 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 controls 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 & Vanderploeg, 2005; Belanger et al., 2010) 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 post-injury, 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 (Broglio & Puetz, 2008; Dougan et al., 2013), but recovery occurs at a much faster rate, with most cognitive domains reaching non-significant effects by seven days post-injury (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 two weeks after the initial injury (Giza & Hovda, 2001; Grindel, 2003), leading Broglio and Puetz (2008) to assess recovery from sports-related mTBI across a 14-day post-injury 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 meta-regression 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 seven days post-injury; however, averaged across domains, a modest effect of mTBI (*d* = .22) remained based on control-group comparisons past these seven days, whereas within-person designs showed full recovery beyond this timeframe (*d* = - .65; Belagner & Vanderploeg, 2005). Comparatively, a more recent meta-analysis (Dougan et al., 2013) identified a slight increase in effect size from 24 hours post-injury (*d* = .38) to 1-10 days post-injury (*d* = .54), but this trend reversed (i.e., *d* = .90 at 24 hours; *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 post-injury 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 post-acute (≥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 at 90 days (Frencham et al., 2005; Rohling et al., 2011), while others have identified nonsignificant effect sizes by 30 to 89 days post-injury (Schretlen & Shapiro, 2003). Despite similar values, Frencham et al. (2005) reported the average acute effect size (*g* = .33) as significantly greater than zero, while the average post-acute effect size (*g* = .28) remained nonsignificant due to greater variability in the post-acute effects. Treating time since injury continuously, cognitive ability improved with time across the

acute phase, but this correlation failed to reach significance in the post-acute phase (Frencham et al., 2005). Other researchers on mixed-mechanism mTBI have provided narrower recovery windows rather than the acute/post-acute dichotomy (Rohling et al., 2011; Schretlen & Shapiro, 2003), identifying consistent improvement across time. Shortly after injury, recovery appears rapid, but decelerates into the post-acute 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 post-injury.

Persistent Post-Acute 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_1 statistic (Cohen, 1988) to quantify the non-overlap 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 post-injury. However, the U_1 value represents the full non-overlap 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 $U_1/2$ 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 post-concussion (McCrea et al., 2003) and 10% of a non-athletic group remaining symptomatic at a one-year follow-up (von Wild, 2008). This subgroup presents a more chronic pattern of symptoms; and, when considered separately from non-symptomatic 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 post-acute phase of mTBI (Kashluba, Paniak, & Casey, 2008), as litigation-based samples increased in symptoms beyond 90 days post-injury while 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 three months post-injury 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 (i.e., gender, athletic competitive level) on neuropsychological outcomes following sports-related mTBI, focusing specifically on these moderators at 1-10 days post-injury among an athletic population. Through an innovative approach, these authors identified 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 meta-regression 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 non-uniform (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 et al. (2009) identified too much heterogeneity in the selected criteria across studies, ranging from established American Academy of Neurology (AAN) 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 (i.e., overly strict or lenient inclusion criteria) or inconsistent operational definitions for each neuropsychological domain. 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 post-injury (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 post-injury (Frencham et al., 2005; Rohling et al., 2011; Schretlen & Shapiro, 2003). Others have posited more rapid recovery windows, specifically among athletes (i.e., seven days, Belanger & Vanderploeg, 2005). Although the average prognosis appears positive, a subgroup of patients with mTBI may remain chronically impaired into the post-acute phase (Frencham et al., 2005; Pertab et al., 2009). While the size (Belanger et al., 2005) and existence (Rohling et al., 2009; Rohling, Larrabee, & Millis, 2012) of this symptomatic group remains debatable, many moderating variables may impact its membership (e.g., compensation-seeking, Kashluba et al., 2008; more severe neurological damage, Levine et al., 2008), but few studies have examined these participants with the needed specificity to fully explain their chronic symptoms (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 to 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 non-athletic 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.

While 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 grey 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., 2009). 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 re-

explore 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 longstanding 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-analyses 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 to 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 relatively 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.

Executive Functions and Intra-Individual Variability following Mild Traumatic Brain Injury

Abstract

The long-term outcomes of executive functions and intra-individual variability (IIV; i.e., trial-to-trial or across-task variability in cognitive performance) following mild Traumatic Brain Injury (mTBI) are unclear due to inconsistent and limited research findings, respectively. Further, the relationship between physical activity (PA) and cognitive performance at young adulthood remains almost fully unexplored. **Objective:** Responding to these gaps in scientific understanding, the current study aimed to (a) assess the diagnostic utility of both executive functions and IIV at predicting mTBI history, and (b) to evaluate the interaction between PA levels and mTBI on both of these cognitive metrics. **Method:** Altogether 138 self-identified athletes (M_{age} = 19.9 ± 1.91 years, 60.8% female, 19.6% 1 mTBI, 18.1% 2+ mTBIs) completed three executive-related cognitive tasks (i.e., N-Back, Go/No-go, Local-Global). Ordinal logistic regression analyses examined the joint effect of person-mean and IIV as predictors of mTBI status. Multi-level models examined mTBI and PA levels as predictors of trial-to-trial changes in performance. **Results:** Only mean response time (RT) for the Local-Global task predicted mTBI status, while no IIV variables reached unique significance. PA levels predicted subtle within-task decreases in RT across Local-Global trials. **Conclusions:** IIV research on mTBI remains limited; however, the preliminary results do not indicate any additional predictive value of IIV indices above mean performances. For executive functions, shifting appears most sensitive to mTBI, with past researchers identifying post-mTBI impairment in attentional processing. Higher PA levels minutely

benefited within-task shifting and mean inhibitory performance, although these finding require cautious interpretation.

Keywords: mTBI, concussion, mild traumatic brain injury, executive function, intra-individual variability, IIV

Introduction

Mild Traumatic Brain Injury (mTBI, often referred to as concussion) has notable deleterious effects on brain functions shortly after injury (Grindel, 2003). However, as most symptoms subside after the acute recovery phase (i.e., three months post-injury; Frencham, Fox, & Maybery, 2005; Rohling et al., 2011), the cognitive sequelae of mTBI have been considered clinically insignificant (Binder, Rohling, & Larrabee, 1997; Shretlen & Shapiro, 2003). Athletes, in particular, exhibit more rapid recovery trajectories and return to baseline by seven days post-injury (Belanger & Vanderploeg, 2005), with physical fitness serving as a potential, but unexplored, moderating variable within this population. Mild TBI occurs at a heightened frequency among physically active populations (Coronado, McGuire, Faul, Sugerman, & Pearson, 2012) and growing public health concern surrounds sports-related concussions (Moser, 2007), with neural atrophy and degeneration occurring among athletes long after retiring from play (Guskiewicz et al., 2005; Lehman, Hein, Baron, & Gersic, 2012; McKee et al., 2009). However, based on past meta-analytic findings, the average post-acute cognitive effect of mTBI appears particularly small (Karr, Areshenkoff, & Garcia-Barrera, in press).

Following these research conclusions, mTBI has become synonymous with rapid symptom resolution. In military mTBI, established concussion treatment algorithms involve expected recovery by seven days (Barth et al., 2010); however, some researchers

have posited that universal symptom resolution appears unlikely, with meta-analytic methods disguising individual differences in post-mTBI cognitive outcomes (Iverson, 2010). Termed the 'miserable minority' (Ruff et al., 1994; Ruff, Camenzuli, & Mueller, 1996), a small group of mTBI patients may remain persistently symptomatic following mTBI (Pertab, James, & Bigler, 2009), emphasizing the need for sensitive neuropsychological metrics to identify subtle subgroup impairments.

Criticism surrounds the sensitivity of neuropsychological tests at detecting long-term post-mTBI impairments (Binder et al., 1997; Broglio, Moore, & Hillman, 2011). However, the small mTBI-related effect sizes associated with cognitive testing performance often derive from collapsed estimates across different mental abilities, although neuropsychological domains vary in terms of post-mTBI outcomes (e.g., Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005; Frencham et al., 2005). As well, for some cognitive abilities, effect sizes vary across meta-analyses, likely due to poor operational definitions of each construct, with independent researchers often allocating the same neuropsychological tests to different domains (Karr et al., in press). Executive functions present the most notable variability across meta-analyses (range: d = -.11 to .72; Belanger & Vanderploeg, 2005; Zakzanis, Leach, & Kaplan, 1999). These higher-order cognitive constructs have historically eluded researchers, as they are both difficult to operationalize (Jurado & Rosselli, 2007) and measure repeatedly (Bartels, Wegrzyn, Wiedl, Ackermann, & Ehrenreich, 2010). In turn, the variability in their associated effect sizes may derive from insufficient operational definitions of executive functions. Research is needed to apply recently established cognitive models to the measurement of these constructs.

Executive Functions

A lengthy history of theoretical and empirical work has established a foundational understanding of executive functions by psychological researchers (Jurado & Rosselli, 2007). A key study within the field identified three latent factors linked to frontal lobe functioning (i.e., updating, shifting, and inhibition) that overlapped in their predictive validity of more complex executive-related tasks, establishing both the diversity and unity of executive functions (Miyake et al., 2000). These three components derive largely from frontal lobe functioning; however, growing evidence supports their reliance on more posterior and subcortical substrates as well (Jurado & Rosselli, 2007). Associated with dorsolateral prefrontal functioning (D'Ardenne et al., 2012), the first component, updating, refers to the manipulation of information in working memory, actively trading old information for more pertinent information related to the current task. The second component, shifting, has been linked to the anterior cingulate cortex (ACC) and represents a function of the anterior attention network (Posner & Rothbart, 2007; Posner, Rothbart, Sheese, & Tang, 2007). This ability involves switching between multiple sets of task demands, overcoming the interference of concurrent or previous task demands to respond accurately to the current stimulus. Lastly, inhibition has been associated with lateral orbitofrontal activity (Rolls, 2004) and refers to the intentional suppression of a prepotent response, where an individual cognitively restricts a dominant response pattern in reaction to an unexpected change in task demands. Altogether, these three factors represent distinguishable, but interrelated cognitive abilities that combine to predict performance on more complex executive-related tasks (Miyake et al., 2000). In turn, the universal term 'executive functioning' refers to a collection of self-regulatory abilities

that work both independently and conjunctively to produce and direct volitional behavior in response to novel cues or environmental requisites.

Although the exact number of executive components remains unclear (Jurado & Rosselli, 2007), the three factors identified by Miyake and colleagues (2000) have become well established and highly cited within the field as replicable factors derived from executive-related tasks (Fisk & Sharp, 2004; Frazer, 2012; Testa, Bennett, & Ponsford, 2012). In relation to mTBI research, no past studies have used an established model of executive functions when selecting cognitive outcomes. Overall, the operational definitions of executive functions among mTBI researchers appear particularly inconsistent, leading to sometime disparate findings (Karr et al., in press). A recent systematic review rated mTBI research based on scientific merit (Comper, Hutchison, Magrys, Mainwaring, & Richards, 2010), with one highly ranked study broadly operationalizing executive functions as performance on one sole measure (i.e., Trail Making Test, Part B; Collins et al., 1999).

An older meta-analysis originally conceptualized mTBI as a frontal-executive pathology (Zakzanis et al., 1999); and more recently, a high-profile autopsy of a retired American football safety showed significant frontal pathology, likely deriving from a history of multiple sports-related mTBI (Roehr, 2012). Although some imaging evidence has linked mTBI to executive dysfunction (Lipton et al., 2009; Niogi & Mukherjee, 2010), past meta-analyses have predominantly found minimal support for long-term executive-related deficits following mTBI (e.g., Belanger & Vanderploeg, 2005; Belanger et al., 2005; Binder, Rohling, & Larrabee, 1997; Rohling et al., 2011); however, others have identified more adverse impacts of mTBI on higher-order cognitive functions

(e.g., Zakzanis et al., 1999; Belanger, Spiegel, & Vanderploeg, 2010; Frencham et al., 2005). Multiple variables appear to moderate this effect, including time since injury (i.e., most athletes return to baseline by seven days post-mTBI; Belanger & Vanderploeg, 2005) and number of past mTBIs (i.e., multiple mTBIs have a greater impact on executive functions; Belanger & Vanderploeg, 2005; Belanger et al., 2010). As noted earlier, this inconsistency may derive from poor operational definitions of executive functions or inadequate sensitivity of neuropsychological tests at detecting long-term impairment. Another potential conclusion concedes that mTBI does not lead to long-term impairment in mean cognitive performance, as concluded by many past meta-analysts (Belanger & Vanderploeg, 2005; Belanger et al., 2005; Frencham et al., 2005; Rohling et al., 2011; Schretlen & Shapiro, 2003); however, meta-analytic findings derive fully from analyses of averaged performances, drawing clinical inference from solely mean outcomes. An alternative method for cognitive assessment involves the examination of intra-individual variability (IIV), or inconsistency in cognitive performance across time or different tests (Hultsch, Strauss, Hunter, & MacDonald, 2008). Past researchers have proposed IIV analysis as valuable for mTBI assessment (Bleiberg, Halpern, Reeves, & Daniel, 1998), but only a limited body of existing research has explored IIV following mTBI.

Intra-Individual Variability

IIV consists of increased response variability, often quantified through an intra-individual standard deviation (ISD) or a similar metric, such as the intra-individual coefficient of variation (ICV; Hultsch et al., 2008). Past researchers have identified many ways of assessing IIV, with inconsistency and dispersion standing as two common

methods. Inconsistency quantifies variability in performance, often recruiting response time (RT) as a trial-to-trial outcome to evaluate variations in within-task performance. Dispersion refers to IIV within a battery of neuropsychological tests, calculated as the ISD of standardized performance scores across multiple cognitive tasks (e.g., Christensen et al., 1999; Hilborn, Strauss, Hultsch, & Hunter, 2009). A developing body of research has begun examining IIV indicators in relation to neuropsychological impairment following TBI, with past researchers positing that increased variability after brain injury represents "a compromised central nervous system struggling to maintain optimal and consistent performance" (Hill & Rohling, 2011, p. 164). Further, the neural substrates of IIV share involvement with executive functions, indicating a potential relationship between higher-order cognitive deficits and increased IIV following head injury.

Multiple executive-related neurological structures and functions overlap with IIV (MacDonald, Nyberg, & Bäckman, 2006), with past researchers linking heightened IIV to frontal lobe lesions (Stuss, Murphy, Binns, & Alexander, 2003). During poor inhibitory performance (i.e., increased errors), IIV positively correlated with increased bilateral activity in the middle frontal gyri, linking IIV to increased executive-related demands (Bellgrove, Hester, & Garavan, 2004). Mild TBI has resulted in axonal injuries within the dorsolateral prefrontal cortex that correlate with deficits in executive-related performances (Lipton et al., 2009); and, in turn, researchers have linked frontal and temporal white matter damage to cognitive deficits post-injury (Niogi & Mukherjee, 2010). Among a non-injured sample, heightened IIV tends to associate with less white matter in the brain (Walhovd & Fjell, 2007), indicating an overlap between myelin integrity and IIV. With some past researchers identifying frontal pathology (Lipton et al.,

2009; Niogi & Mukherjee, 2010) and executive dysfunction following mTBI (Belanger et al., 2010; Zakzanis et al., 1999), IIV may co-occur with executive-related deficits; however, only one past study has explored IIV in executive functions post-mTBI (Halterman et al., 2006) and overall few past mTBI researchers have explored IIV for any cognitive outcome.

Research on IIV has steadily developed over the last two decades, focusing primarily on cognitive aging (Hultsch et al., 2008). Only one past meta-analysis has examined IIV, but it covered neither TBI nor executive functions (Dykiert, Der, Starr, & Deary, 2012). These authors examined age-related IIV increases in simple and choice RT tasks, identifying larger effect sizes for the more complex choice-based tasks. The aging research on IIV has reached a greater overall maturity than TBI research, but IIV may provide a meaningful metric for assessing cognitive performance following TBI (Hill & Rohling, 2011). In turn, preliminary research has demonstrated some TBI-related increases in IIV across grades of injury (Hultsch et al., 2008). Although too few studies for a meta-analysis, several articles have examined IIV following mTBI (Bleiberg, Garmoe, Halpern, Reeves, & Nadler, 1997; Burton, Hultsch, Strauss, & Hunter, 2002; Halterman et al., 2006; Hill & Rohling, 2011; MacFlynn, Montgomery, Fenton, & Rutherford, 1984; Makdissi et al., 2001; Sosnoff, Broglio, Hillman, & Ferrara, 2007; Stuss et al., 1989), described in detail in Table 7.

The first study examining mTBI-related IIV identified significantly greater RT variability among concussed participants when compared to controls within 48 hours of injury, but this difference subsided by 6 weeks post-mTBI (MacFlynn et al., 1984). These authors used the ICV as their IIV index (i.e., ISD divided by individual mean RT), but

this method does not fully control for main effects deriving from mean performance that may underlie IIV group differences (Hultsch et al., 2008). Similarly, Stuss et al. (1989) found significantly greater RT ISDs than control participants; however, these researchers collapsed concussed participants with more severe TBI participants, blurring the interpretability of their results. These researchers also failed to account for mean confounds in their analyses, with their findings potentially deriving from mean group differences, as higher individual means (i.e., slower RT) are often significantly correlated with higher ISDs (Jensen, 1992).

Nearly a decade after these findings, Bleiberg et al. (1997) examined a small group of mild/moderate TBI participants, identifying increased variability for head-injured participants proportional to median slowing in RT. Sequential studies evaluating IIV have found similarly null results, including no increase in IIV – as measured by ICV – for an attentional task involving an executive component (Halterman et al., 2006) and no unique IIV group differences in RT once controlling for mean post-mTBI performance (Sosnoff et al., 2007). In a small prospective study ($N = 6$), researchers identified increased IIV post-mTBI and decreased IIV among non-injured control participants at follow-up, labeling RT variability as a notable deficit following concussion (Makdissi et al., 2001). Notably, these researchers also failed to control for mean RTs in their repeated measures analyses. One additional study reported heightened IIV post-mTBI, assessing IIV in physical functioning, stress and affect across weeks (Burton et al., 2002). Without adjusting for person-mean differences, these researchers identified greater variability in solely right-hand grip strength among mTBI participants, a fairly trivial conclusion with limited clinical value.

Aside from trial-to-trial assessments of IIV, one research group examined dispersion within a database of TBI patients (i.e., IIV across standardized performance scores for a battery of cognitive tests), identifying increased IIV with greater TBI severity (Hill & Rohling, 2011). Across four TBI categorizations based on loss of consciousness (LOC) duration, brain injuries with LOC under an hour – the group most analogous to mTBI – presented the lowest IIV and highest mean performance for the neuropsychological test battery; however, without a non-injured control group for comparison, it remains unclear whether the observed mTBI-related dispersion levels differ from normally occurring performance variability across cognitive tasks. Another study explored dispersion among athletes both before and after concussion (Rabinowitz & Arnett, 2013), identifying no changes in IIV or overall cognitive performance post-concussion. A cluster analysis identified athletes with higher baseline dispersion tended to increase in IIV post-concussion; however, this conclusion derived from solely a statistical trend.

Overall, the existing IIV research remains preliminary, with conflicting conclusions and diverse methodology. Notably, the limited control for mean confounds across studies ignores the high correlations that frequently occur between ISDs and individual means (Jensen, 1992). In turn, it remains unclear whether the heightened IIV among past mTBI participants (Bleiberg et al., 1997; Burton et al., 2002; MacFlynn et al., 1984; Makdissi et al., 2001; Stuss et al., 1989) represents unique and informative phenomena or merely reflects underlying mean RT differences. These disparate results parallel the diverse measurements of executive functions across studies and their incongruent effect sizes across meta-analyses (Karr et al., in press). Further confounding

these past findings, many previous mTBI studies have focused on athletic samples (Broglio & Puetz, 2008; Dougan, Horswill, & Geffen, 2013) and physical fitness could moderate the cognitive outcomes of mTBI; however, this variable remains unexplored by past researchers (Belagner & Vanderploeg, 2005). With the considerable prevalence of mTBI among athletic populations (Coronado et al., 2012), physical fitness may affect executive functions among young and active participants (Hillman, Erickson, & Kramer, 2008), potentially impacting the results of past researchers.

Physical Fitness and Cognition at Young Adulthood

Considering the growing evidence on neuroplasticity following TBI, exercise has gained empirical support as a holistic intervention, promoting brain health among those at risk for neurodegeneration and atrophy (Griesbach, 2011; Griesbach, Hovda, Molteni, Wu, & Gomez-Pinilla, 2004). Focusing on executive functions, physical fitness has reportedly buffered against declines in populations at risk for executive-related deficits (e.g., dementia), likely due to neural changes (e.g., neurogenesis, vascularization; Hötting & Röder, 2013) that result from active lifestyles (Heyn, Abreu, & Ottenbacher, 2004; Larson et al., 2006). Exercise early in life has predicted cognitive outcomes at later ages, inferring that a resilient neuromodulation occurs through physical activity (Middleton, Barnes, Lui, & Yaffe, 2010). Similar to older populations, some evidence suggests that exercise improves executive functions at younger ages as well, including adolescence (e.g., Stroth et al., 2009, 2010) and adulthood (Masley, Roetzheim, & Gualtieri, 2009). The only study evaluating young adults found a positive correlation between cardiovascular fitness and global intelligence, but did not examine specific executive-related abilities (Aberg et al., 2009). Overall, few studies have explored the cognitive

benefits of exercise beyond childhood and prior to adulthood (Hillman, Erickson, & Kramer, 2008); however, the preliminary evidence demonstrates a potential relationship between these variables prior to later age.

Perceivably, any fitness-based cognitive change may buffer against the cognitive detriments of an adverse neurological event, such as an mTBI. Among cases of sports-related mTBI, physical fitness remains an unexplored moderator, despite heightened physical activity levels characterizing this population (Belanger & Vanderploeg, 2005). As physical exercise benefits cognitive performance (Hillman et al., 2008), the fitness gained by young adults through athletics may moderate the potentially adverse impact of mTBI on executive functions and IIV.

Research Aims and Hypotheses

The long-term outcomes of executive functions and IIV following mTBI appear unclear due to inconsistent and limited research findings, respectively. Further, the relationship between physical activity and cognitive performance during young adulthood (i.e., between adolescence and adulthood) remains almost fully unexplored. Responding to these gaps in scientific understanding, the current study aimed to (a) assess the diagnostic utility of both executive functions and IIV (i.e., inconsistency and dispersion) at predicting mTBI history, and (b) to evaluate any interaction between physical activity levels and mTBI on both of these cognitive metrics. In turn, we hypothesized both executive functions and IIV would uniquely predict mTBI group membership among an athletic sample believed to be fully recovered (i.e., past seven days post-injury; Belanger & Vanderploeg, 2005; Barth et al., 2010), with physical activity levels buffering against the conceivably adverse impact of mTBI on cognitive outcomes.

Method

Participants

Recruitment targeted university-aged athletes from a psychology research participant pool, with a total of 138 university students participating in this study (M_{age} = 19.9 ± 1.91 years, 60.8% female), including 86 without mTBI (M_{age} = 19.9 ± 1.62 years, 62.8% female), 27 with one past mTBI (M_{age} = 19.85 ± 2.07 years, 63.0% female) and 25 with two or more past mTBIs (M_{age} = 20.0 ± 2.63 years, 56.0% female). As recruitment targeted self-identified athletes, sports affiliations remained particularly heterogeneous, with several athletes reporting multiple sports affiliations. Across the 138 participants, 59.4% reported affiliations with aerobic sports (e.g., swimming, rowing, cross country), 55.8% with court/field sports (e.g., volleyball, tennis), and 65.2% with head-contact sports (e.g., hockey, rugby, boxing, soccer). These affiliations included either recreational or intercollegiate competitive levels. The percentages sum to greater than one hundred due to athletes reporting affiliations across multiple categories.

Participants with mTBI reported a history of one or more concussions. The mTBI variable was collapsed into three sequential categories, representing 0, 1 and 2+ self-reported mTBI to avoid overestimates of past mTBI frequencies. Deficits in executive functions appear most common in comparisons of multiple mTBI groups over single mTBI groups (Belanger et al., 2010), rationalizing the trichotomous coding over a dichotomous concussed versus non-concussed group comparison. Among athletes with mTBI, 50% reported at least one mTBI involving LOC. The average time since injury was particularly heterogeneous at 38.47 ± 41.59 (range: .69 to 166.19) months. Exclusion criteria included uncorrected vision problems, history of neurological disorder or brain

injury other than concussion, and a concussion less than seven days prior to testing (Belanger & Vanderploeg, 2005; Barth et al., 2010).

To improve the homogeneity of mTBI cases, a second series of effect size comparisons selected a subsample of mTBI participants reporting a single LOC concussion (N = 15; M_{age} = 19.9 ± 2.44 years, 53.3% female) or two or more LOC concussions (N = 11; M_{age} = 21.0 ± 3.20 years, 45.5% female), classified as Grade III mTBI based the American Academy of Neurology criteria (Kelly et al., 1997). Combined, these groups presented a mean time since injury of 34.77 ± 37.13(range: .82 to 152.91) months. In addition, a subsample of control participants was randomly selected from the non-injured participant group (N = 15; M_{age} = 19.9 ± 2.13 years, 66.7% female). This project received full approval by the University of Victoria institutional ethics review board (Ethics Protocol Number 11-451).

Materials and Procedure

Participants scheduled appointments for testing sessions on the University of Victoria campus through an online participant recruitment system. Once participants provided signed consent, they completed a short history questionnaire and five computerized tasks (only three tasks were assessed in the current analyses). All tasks lasted approximately forty-five minutes. The short questionnaire covered personal information, sports affiliations, physical activity levels, and mTBI history. The questionnaire served to collect basic participant information (e.g., age, gender), assess participant eligibility, and document typical exercise levels and mTBI history. As the recruitment did not track specific sports teams, the Short-Form International Physical Activity Questionnaire (IPAQ; Hagströmer, Oja, & Sjöström, 2006) quantified the

physical activity levels within the sample, categorizing between high, moderate, and low activity participants under established IPAQ Research Committee (2005) guidelines.

Cognitive tasks. Outcome measures consisted of computerized tasks previously validated as indicators of theoretical executive functions. The tasks were programmed and administered using MatLab R2012b v.8 software package and Psych Toolbox. The selected measures represented specific constructs posited as higher-order cognitive factors by past researchers, including the N-back task for the updating of working memory (Miyake et al., 2000), a Local-Global task for shifting (Navon, 1977), and a Go/No-go task for inhibition (Donders, 1868/1969). The N-back involved keeping track of a sequence of letters appearing on a computer screen, with participants responding by pressing a key when the letter displayed in the sequence matched the letter displayed two back in the same sequence. Each letter stimulus was displayed for 750 ms, separated from the following stimulus by a 750 ms display of a + symbol (e.g., N, +, B, +, N). The outcomes for this measure included accuracy and RT for each trial eliciting a response.

The Go/No-go involved two response blocks. For Block I, participants responded as quickly as possible to all presented stimuli, eliciting a prepotent response. Each new stimulus was displayed for 750 ms. Successive stimuli were separated by a blank screen with duration uniformly and randomly distributed between 600 ms and 800 ms in order to prevent rhythmic responding. Block II involved participants responding to all stimuli except one target (i.e., the letter ‘J’ appearing for 20% of the trials). The timing for Block II was identical to that of Block I. The outcomes for this measure included Block II accuracy and trial RTs for both blocks. Block I RT produces a measure of simple RT,

whereas Block II RT presents longer latencies due to the potential for inhibited responses, adding an executive component to the task demands.

The Local-Global involved three response blocks, with each stimulus displayed until the participant elicited a response. During Block I, participants saw shapes and responded with the number of sides of the shape. Similarly, during Block II, participants saw colored shapes and responded based on color. Lastly for Block III, participants saw colored shapes composed of smaller shapes of the same color, responding with the number of sides of either the smaller or the larger shapes based on the color of the full design. The outcomes for this measure included accuracy and RT for all blocks, with the RT for Block III presenting longer latencies due to the additive executive-component of switching required across trials.

Statistical Analyses

To achieve the study aims, performance on the cognitive battery was assessed via three methods, including multilevel modeling (MLM), ordinal logistic regression, and effect size comparisons. Due to limited power for hypothesis testing, only the effect size comparisons were conducted for the LOC subsample analysis. Beginning with MLM, this approach evaluated change in within-task performance across trials, assessing predictors of linear and quadratic slopes quantifying that change for each cognitive outcome. All MLM analyses described in the following section were conducted using HLM v.6 (Raudenbush, Bryk, & Congdon, 2004) and all ordinal regression analyses were conducted using MPlus v.6.12 (Muthén & Muthén, 2011).

MLM Approach. Three parallel MLM models separately assessed performance on each executive task, with trial RT as the outcome. For the N-back, the RT values were

derived from target trials eliciting a response; whereas, for the Go/No-go and Local-Global tasks, the RT values derived from the response trials of Blocks II and III, respectively (i.e., the Blocks involving additive executive-related task demands). RT values for both correct and incorrect trials were included in analysis, adjusting for accuracy through its use as a predictor in the model. This method was considered more parsimonious than the exclusion of incorrect trials, as the latter would result in significantly more non-random missingness for less accurate participants

Focusing first on level-1 predictors, the MLM approach used trial as the time metric, recoded so that a zero value indicated the central trial in the task series (i.e., this strategy limits colinearity with linear and quadratic parameterizations). Two tasks involved trials eliciting no responses (i.e., N-Back, Go/No-go), with these no-response trials deleted from their respective datasets to avoid maximum likelihood value estimations of RT outcomes for cells with non-random missingness. Remaining trials retained trial numbers that aligned with their actual presentation in the sequence (i.e., trial 40 remained trial 40, even if preceding trial values were deleted).

The models would only converge with two or fewer estimated random effects. As the intercept represented the central trial in the task series, its variance had limited ecological meaning. In turn, random effects were estimated for only slope and quadratic trends for each outcome. Separate models estimating random effects for the intercept and linear or quadratic slope were run to evaluate individual differences in RT levels that were masked when fixing the intercept to a common value. Where relevant, these findings are discussed in the results section.

Level-2 variables predicted both slope and quadratic estimates by following a model building approach with three sequential models adding additional variables. The first model included only control variables specific to each task (i.e., N-Back: Accuracy; Go/No-go: Block I mean RT, Block II Accuracy; Local-Global: Blocks I-II mean RT, Blocks I-III Accuracy). By controlling for this set of predictors, variables added in later models effectively predicted the variance in the slopes not attributable to specific task accuracy or preliminary Block RT performances (i.e., solely the added executive component of the task measurable through RT of the outcome trial block).

The second model included physical activity levels and total self-reported mTBIs as predictors. Low, moderate and high physical activity levels along with 0, 1 and 2+ self-reported mTBI were coded as 0, 1 and 2, respectively. The third model included a physical activity levels by total self-reported mTBI interaction, representing the synergistic impact of these variables on each executive-related outcome. To compare adjusted models with additional parameters to nested models, changes in fit were assessed via chi-square difference testing of the -2 Log Likelihood (-2LL, also known as deviance) with decreases in -2LL values indicating improved model fit.

IIV analyses. The ISD has become a common metric for IIV research, representing the within-person variance in trial-to-trial performance. As no best-practice method for ISD calculation exists, three ISD estimates were calculated for each outcome: the raw ISD, the MLM ISD, and the residualized ISD. Prior to ISD calculation, all trial RT scores were converted to *T*-scores to produce only positive and interpretable variability estimates. Raw ISD was calculated as the SD of the unadjusted RT scores across trials, whereas two alternative statistical techniques extracted the MLM and

residualized ISDs from the dataset, through either an MLM detrending approach or an ordinary least squares (OLS) residualization technique. The MLM approach regressed within-person predictors on the outcome at each trial, producing level-1 residuals detrended for linear, quadratic and cubic parameters. As level-2 predictors do not directly impact level-1 residuals in MLM, this approach does not partial the systematic variance of between-person predictors, removing solely within-person variance from the residual RT values.

The OLS approach produced the residualized ISD, using both within-person (i.e., trial order and its higher-order polynomials) and between-person predictors (i.e., mTBI status, individual mean performance, task accuracy) along with their cross-level interactions in linear regression models. This method saves residual trial scores as a newly constructed variable representing an unsystematic portion of variance not accounted for by mean, practice, or group variables (Hultsch et al., 2008).

With the trichotomized mTBI status variable serving as the outcome, a series of ordinal logistic regression analyses evaluated the unique predictive quality of IIV indicators over performance-level variables (i.e., accuracy, mean RT). For each executive-related measure, separate hierarchical regression procedures entered additional variables into the model. For each outcome, Model 1 contained only control variables, including accuracy for the N-Back, mean Block I RT for the Go/No-go, and Block I/II mean RT and accuracy for the Local-Global. Model 2 added meaningful performance indicators, including mean RT for the N-Back, Block II accuracy and mean RT for the Go/No-go, and Block III accuracy and mean RT for the Local-Global. Lastly, for Model 3, each ISD value (i.e., raw, MLM and residualized) was included in a separate and

identical model, evaluating differences in the unique effects of each predictor. The ISDs derived from N-Back RT, Go/No-go Block II RT and Local-Global Block III RT. Evaluation of each model focused on the unique significance of each predictor, with significance set at $p < .05$. In addition, ΔR^2 values were assessed to examine the amount of explained variance associated with each added predictor or variable set.

An additional analysis focused on dispersion across the three executive tasks, involving performance measures for each outcome (i.e., N-Back, accuracy; Go/No-go, Block II RT - Block I RT; Local-Global, Block III RT - mean Block I/II RT). The N-Back accuracy was re-coded so that a higher score indicated worse performance. As with the trial RT data, all scores were standardized and converted to *T*-scores prior to the calculation of an average performance and ISD for the executive function task battery. Two sequential ordinal logistic regression models evaluated the prediction of mean performance and dispersion on the number of past mTBIs, with the first model including only the average *T*-score for the battery and the second model adding the across-task ISD as an additional predictor.

Effect Size Comparisons. As small sample size introduces bias against null results during logistic regression (Nemes, Jonasson, Genell, & Steineck, 2009), the LOC subsample lacked sufficient power for independent logistic regression analyses. In turn, the assessment of this subsample remained purely measurement-based rather than inferential, focusing on effect size comparisons rather than hypothesis testing. Effect sizes, *d* (Cohen, 1988), and 95% Confidence Intervals (CIs) were calculated for both the full sample and LOC subsample, identifying any differences based on operational

definitions of mTBI. All effect sizes and 95% CI were calculated using Effect Size Generator v.2.3 (Devilly, 2004).

Data Preparation

For trial-to-trial data on each measure, RT scores under 150 ms were excluded, based on previously established lower-bound cutoffs recruited for IIV analyses involving young adults (Hultsch, MacDonald, Hunter, Levy-Bencheton, & Strauss, 2000). Thereafter, outliers were removed from within-participant performances based on a +/- 3 standard deviation cutoff criterion deriving from individual participants' mean scores. Combined with participant non-responses for some target trials, this process resulted in varying degrees of missing trial values across outcome variables (i.e., 32.3% N-Back, 17.6% Local-Global, 4.4% Go/No-Go), but the removal of these extreme data points ultimately provides a more conservative estimate of variability.

Results

Table 5 summarizes the descriptive statistics of mean performances and ISDs for each executive-related outcome based on the number of past mTBIs for both the full sample and the LOC subsample. As well, Table 6 provides the correlations between IIV and mean RT outcomes for each cognitive task and time since injury. As displayed in the correlation matrix, relationships between variables differed across the full and LOC samples. Intra-task correlations were consistent across each sample, and most notably the ISDs significantly correlated with mean RTs for each measure. This correlation appeared highest within the Local-Global, correlating at .858 among the full sample. Notably, time since injury did not correlate with any cognitive measures for mTBI participants,

indicating the sample had passed the acute recovery phase. Physical activity levels presented a modest correlation with Go/No-go accuracy among the full sample (r = .192) and Go/No-go RT among the LOC subsample (r = -.381); however, these small correlations remain susceptible to Type I error and require cautious interpretation.

MLM Findings

Across outcome variables, intra-class correlations (ICC) for the fully unconditional model showed only a modest amount of variance attributable to between-person variability (i.e., .235 N-Back, .181 Local-Global, .414 Go/No-Go), indicating that most model variance derived from within-person fluctuations in RT across trials. Table 7 lists the fixed and random effects across each model for each outcome. As the control variables included in Model 1 lack inferential meaning, the specific estimates for these predictors are not listed in the table. Notably, the sole control variable for the N-Back (i.e., accuracy) reduced the slope variance to a non-significant value; however, to parallel the model building approach for other executive outcomes, the slope was still predicted by additional variables in later models. For Model 2, the mTBI and physical activity level variables did not improve model fit for either the N-Back or Go/No-go, indicating no influence of these variables on task performance. However, for the Local-Global, Model 2 showed significant improvement in fit over Model 1.

Physical activity levels trended towards significance for this model when predicting slope (β = -.001, p = .062), indicating that slope slightly decreased with increased physical activity. Total mTBIs did not significantly predict the linear slope, but did predict the quadratic slope (β =.000083, p = .002). For the Local-Global, the overall quadratic trend was negative, signifying an inverted U-shaped curve in trial RT

performance on average across the sample (i.e., a downward curve in trial RT mid-task). Although a very small estimate, the positive quadratic β-weight for mTBI status indicated an increasingly U-shaped trend with a greater number of past mTBIs. Based on this trend, RT would have decreased during earlier trials (i.e., learning), but showed a gradual slowing at later trials (i.e., fatigue). However, the slope variances accounted for by Model 2 could not be reliably calculated due to already extremely small random effect estimates in Model 1, suggesting an otherwise minute effect size. In turn, the variance accounted for by Model 2 was so small that performances between different mTBI groups could not be visibly differentiated on a line graph.

When interpreting these findings, the quadratic effect may be confounded due to constricted performance levels mid-task, as the random effect for intercept was not estimated. A model estimating random effects for the intercept and quadratic slope would not converge; and consequentially, it remains unclear whether mTBI status would remain a significant predictor of the quadratic trend in a model without a fixed intercept. Notably, a Local-Global model with random effects for the intercept and linear slope, but not the quadratic trend, found that mTBI status significantly predicted intercept ($\beta = .101$, $p = .031$). Based on this estimate, the intercept slightly increased with each additional self-reported mTBI, indicating higher mean RT (i.e., worse performance) due to mTBI at mid-task (i.e., the central trial was coded as the intercept). These individual differences are constrained in the models estimating variance components for solely the linear and quadratic trends.

Significant random effects for both linear and quadratic slopes remained for the model after the inclusion of all predictors, while reliability estimates for the linear ($r =$

.293) and quadratic slope (r = .872) indicated higher proportions of variation between participants in the quadratic trend. Noting these distinct reliability values, tau correlations between slopes remained particularly low (r = .066), suggesting a minimal relationship between individual differences in linear and quadratic performance patterns across the task. The addition of the mTBI by physical activity level interaction in Model 3 showed no uniquely predictive quality for any outcome nor any improvement in model fit. As well, in the presence of the interaction terms, the conditional main effects for the mTBI and physical activity predictors did not reach significance for any outcome.

IIV Outcomes

Aside from lower variability estimates associated with raw ISD, the MLM and residualization methodologies for ISD calculations produced analogous values across outcomes. This similarity likely derived from the low ICC values described earlier, implying that the majority of variance derived from within-person sources. In turn, the additive control for between-person confounds associated with the residualization approach presented no inferential advantage within this dataset.

Pertaining to the logistic regression models, Tables 8-10 report the estimates for each model across all executive outcomes. Neither mean performances nor IIV indicators significantly predicted the number of past mTBIs for either the N-back or the Go/No-go tasks. These analyses indicated only one uniquely significant predictor of the polytomous mTBI outcome: mean RT for Block III of the Local-Global task. For every one unit increase in RT for this task, the model presented a 1.52 increase in the logit of moving from fewer mTBI to a higher ordinal category, given that all other variables are held constant. This estimate increased with the addition of any form of ISD into the model

(i.e., raw, MLM, or residualized), indicating that ISD accounted for some unique variance in the categorical outcome, but not enough to reach significance. Concerning explained variance, the addition of mean Block III RT for the local-global accounted for a modest portion of variance (i.e., $\Delta R^2 = .163$), whereas the addition of ISDs into the model produced much smaller changes in explained variance ($\Delta R^2 = .043$ to .083, depending on ISD calculation). Dispersion analyses identified neither average test performance nor test battery variability as significantly predictive of number of past mTBIs.

Effect Size Comparisons

A forest plot in Figure 3 schematically illustrates effect sizes and 95% CIs across samples, tasks and outcomes. All effect sizes were coded with negative values indicating worse performance for participants with a greater number of past mTBIs. Only the full sample presented effect sizes with 95% CIs that did not overlap the zero demarcation. Although the Go/No-go did not predict mTBI status, its effect sizes for mean RT (d = -.47) and ISD (d = -.62) appeared reliably different from zero and showed worse performance of single mTBI participants when compared to non-injured participants. Also based on non-injured to single mTBI comparisons, the Local-Global presented worse performance for the mTBI group on ISD with an effect size reliably distinct from zero (d = -.47); however, the 95% CI for its mean RT effect size (d = -.42) slightly overlapped the zero demarcation, but trended towards worse performance for single mTBI participants. Among the LOC subsample, the 95% CI for the mean Local-Global RT effect size (d = -.79) also slightly overlapped zero, but trended towards worse performance for the 2+ mTBI group over the single mTBI group.

Discussion

Examining three established executive functions (Miyake et al., 2000), shifting performance best differentiated between groups based on self-reported histories of past mTBI status, although group differences presented fairly minute effect sizes. Overall, mean RT performance on the Local-Global task served as the only significant predictor that uniquely distinguished between non-injured participants and those reporting past mTBIs. Neither tasks of inhibition nor updating presented group differences based on mTBI status, implying distinct post-acute outcomes across executive functions based on history of minor head injuries. In turn, past meta-analyses may have masked the diversity of executive-related outcomes when collapsing effect sizes for higher-order cognitive tasks into a single neuropsychological domain. Across tasks, the non-injured to single mTBI effect sizes for mean RT ranged in magnitude from zero to medium in size (range: d = .01 to -.47). If averaged, the overall effect size becomes quite small (d = -.29), conforming to similar estimates reported by past meta-analyses for executive functions (Belanger et al., 2005; Frencham et al., 2005; Rohling et al., 2011). In turn, the current results match meta-analytic conclusions for a unitary executive construct, but also demonstrate the diverse sensitivity of each executive function to past mTBI.

Contrary to logistic regression results, effect size evaluations of mean RT and ISD for the Go/No-go task indicated worse performance for participants reporting a single mTBI when compared to non-injured participants; however, these measurement-based comparisons did not control for relevant variables (i.e., Block I RT, accuracy). Together, the inhibition and updating tasks did not elicit any group differences, while the frontally-mediated attentional process of shifting appeared specifically sensitive at detecting group

differences. The sensitivity of the shifting task may derive from its overall difficulty compared to the other two executive tasks. Notably, the Local-Global showed a much slower mean RT compared to the other two tasks, demonstrating slower performance likely due to difficulty with shifting. The N-Back (i.e., only a 2-Back task in the current design) and Go/No-go presented fairly quick average RTs (i.e., .30 to .40 seconds) when compared to Local-Global performance (i.e., over 1.5 seconds). This discrepancy may indicate that the prior two tasks did not sufficiently challenge the young and otherwise cognitively healthy participants. In turn, both inhibition and updating may be sensitive to mTBI, but their respective measures did not strain these abilities enough to elicit any group differences.

Despite limitations surrounding task difficulty, the group differences in shifting performance appear consistent with two past research findings, assessing attentional processes following mTBI. These researchers identified similarly null IIV results alongside impairments in anterior attentional networks (Halterman et al., 2006; Sosnoff et al., 2007). The ACC is involved in executive attention (Posner & Rothbart, 2007; Posner et al., 2007) as part of the neural circuit regulating shifting processes (Miyake et al., 2000). As proposed by past researchers, "it appears that the ACC may be particularly susceptible to injury via mTBI and the damage created may take more time to resolve relative to the other attentional components localized to different regions of the brain" (Halterman et al., 2006, p. 752). Sequentially, although past researchers have linked IIV with many frontal processes (MacDonald et al., 2006), no past findings have implicated the ACC in heighted variability, implying that the potential executive-related

impairments linked to mTBI may derive from neurological systems distinct from those eliciting response variability.

As additional evidence for attentional differences based on concussion history, a subtly more positive quadratic trend occurred across Local-Global trials with a greater number of past mTBIs, indicating a decrease in RTs during earlier trials and an increase in RTs during later trials. This performance pattern could demonstrate within-task mental fatigue among mTBI participants, which serves as a common complaint for individuals with past concussions (Stulemeijer et al., 2006). In TBI, fatigue may represent an increase in the psycho-physiological costs of maintaining stable performance (Ziino& Ponsford, 2006), with more difficult tasks likely resulting in depreciated performance at later stages. As well, researchers have linked mental fatigue to impaired processing speed and divided attention (Johansson, Berglund, & Rönnbäck, 2009), with both of these abilities underlying RT performance during the Local-Global task. In turn, the strain of shifting costs may have a greater impact on participants with past mTBI. However, the significant regression weight observed for the quadratic slope proved very small, and its variance components – although significant – were so low that effect sizes were non-calculable. In turn, the finding requires highly cautionary interpretation, but indicates the potential value of exploring trial-to-trial performance patterns rather than mean outcomes when assessing mTBI.

IIV following mTBI

IIV indicators presented no unique differences across groups for any measure, aligning with many past research findings evaluating IIV post-mTBI. Among most studies identifying increased IIV following concussion (Bleiberg et al., 1997; Burton et

al., 2002; Makdissi et al., 2001; Stuss et al., 1989), none have analytically controlled for mean confounds, while those that did produced opposite conclusions (Halterman et al., 2006; MacFlynn et al., 1984; Sosnoff et al., 2007). Two studies proposing heightened IIV reported proportionate increases of IIV with slowing RT performances (Bleiberg et al., 1997; Makdissi et al., 2001), indicating that increased IIV likely depended on slowing RT within these samples.

Within the current sample, the single head injury group presented greater IIV during a shifting task than the non-injured participants, as demonstrated by effect size comparisons; however, this group difference provided no unique additional information beyond mean RT performance, which correlated with its ISD at .858 for the full sample. Increased variability often occurs in conjunction with worsened mean performance (Crawford & Garthwaite, 2006). In turn, "it seems that the vigilance lapses [referring to IIV] are unlikely to be a major feature in the long term recovery from minor head injury," as posited by the first researchers evaluating post-mTBI variability (MacFlynn et al., 1984, p .1330). As with trial-to-trial inconsistency, dispersion did not differentiate between mTBI and control participants, as largely shown in the acute post-concussion phase as well (Rabinowitz & Arnett, 2013); and sequentially, dispersion levels for mTBI patients may not differ from individuals without head injury, likely indicating that only more severe TBIs are linked to increased dispersion (Hill and Rohling, 2011).

Physical Activity Levels

With increased self-reported physical activity, participants tended towards more negative slopes on the Local-Global task, suggesting a more rapid learning curve among more active participants. As well, physical activity levels positively correlated with

Go/No-go accuracy and negatively correlated with Go/No-go mean RT for the full and LOC samples respectively, although these correlations were quite modest. The analyses did not demonstrate an interaction between fitness and mTBI for any outcome, implying no relationship between physical exercise and the cognitive sequelae of mTBI. However, the group differences in cognitive functioning appeared quite small within the current sample and physical fitness may have a more prominent effect closer to injury, which would explain the quicker recovery trajectories among athletes (Belanger & Vanderploeg, 2005) compared to the general population (Belanger et al., 2005; Frencham et al., 2005).

Overall, the observed physical activity benefits were modest and require cautious interpretation. The physical activity levels measured in the current study served solely as a proxy to true physical fitness. The IPAQ has received criticisms for inadequately quantifying activity levels (Lee, Macfarlane, Lam, & Stewart, 2011), as self-reports have often differed from direct measurement (Prince et al., 2008). However, these preliminary results do add to a very small body of research on fitness and cognition among adolescents and emerging adults. To date, the research remains limited, but promising. Most researchers have identified benefits of physical fitness on executive functions (Masley et al., 2009; Stroth et al., 2009, 2010), while only one treatment study found no such benefit (Zinke, Einert, Pfennig, & Kliegel, 2012).

Statistical Limitations

Due to the number of statistical analyses conducted, the experiment presented particularly high error rates for each outcome, nearly guaranteeing at least one false-positive finding. The experiment-wise error rates (EER) were calculated for analyses

examined based on inference, rather than all analyses run (e.g., *p*-values for control variables were not interpreted and therefore not considered in the EER calculation). For the MLM analyses, the EER reach .26 for each outcome variable, with six inferential predictors per outcome (i.e., physical activity, mTBI status and their interaction for both the linear and quadratic trend). For the ordinal logistic regression the EERs were .19 for each outcome variable, with four inferential predictors per outcome (i.e., mean RT and each ISD computation). For the correlation matrix, the EER reached .99, indicating a high likelihood of spurious correlations reaching significance. In addition to false-positive results, false-negative results may have explained the predominantly null findings of the current study due to limited power. The small sample size potentially impeded the detection of group differences; however, as noted earlier, small sample size often introduces bias against null results during logistic regression (Nemes et al., 2009), supporting the accuracy of the current findings.

Design Limitations and Future Directions

The top research on mTBI often involves prospective designs tracking athletes from preseason baselines through post-mTBI assessments (Comper et al., 2010). In turn, the current study appears limited through its use of retrospective reporting of mTBI and open sampling of self-identified athletes. The sampling method limits the generalizability of these findings, as the sample consisted of a homogenous group of similarly aged, active athletic participants with at least some exposure to higher education. As well, the high prevalence of LOC within the sample indicates bias in terms of self-selection, as the majority of mTBIs among athletes do not involve LOC (McCrory et al., 2013). In turn, when relying on self-reports of mTBI, participants likely present a high false-negative

rate as well, with many potentially experiencing unidentified lower grade concussions in the past.

Although many past researchers have used self-reports of mTBI (e.g., Broglio, Ferrara, Piland, & Anderson, 2006; Bruce & Echemendia, 2009; Collins et al., 1999; Iverson, Brooks, Lovell, & Collins, 2006), the reliance of self-report decreases the diagnostic rigor of concussion, as actual times since injury and injury severity remain fairly subjective. To decrease the variability in injury grade, the LOC subsample drew effect size comparisons for a more homogenous sample, but identified no effect sizes reliably distinct from zero (i.e., only one trend for mean Local-Global RT), potentially due to insufficient sample size producing wider CIs. Many operational definitions for concussions have been applied by past researchers (Comper et al., 2010), with variable rigor in diagnostic criteria (Pertab et el., 2009). Ultimately though, reliance of self-report results in significant heterogeneity of mTBI diagnoses, times since injury and sports affiliations, which cumulatively limits the purity of group comparisons.

The limitations of self-report have commonly occurred with studies involving samples reporting multiple mTBIs (Belanger et al., 2010). In the current study, the multiple mTBI group appeared particularly inconsistent and often presented better performances than control or single mTBI participants. Past meta-analyses have reported the most prominent effects of repeated mTBI on executive functions (Belanger & Vanderploeg, 2005; Belanger et al., 2010), while the current study found only a 5 ms increase from single to multiple mTBI for the Local-Global task (d = -.11). Similarly, the control group differed from the single mTBI group by only 200 ms on average (d = - .42). In turn, the impact of this RT difference on everyday functioning remains questionable.

As well, it appears unclear whether this observed executive deficit serves as evidence for long-term cognitive impairment or merely an artifact of preexisting group differences unidentified by the cross-sectional design. In turn, future researchers must explore the diverse outcomes of executive functions prospectively from preseason baselines to post-mTBI assessments, identifying whether dysfunctions in executive attention underlie the persistent cognitive deficits and fatigue following mTBI.

Cited Figures

Figure 1. Flowchart of systematic review

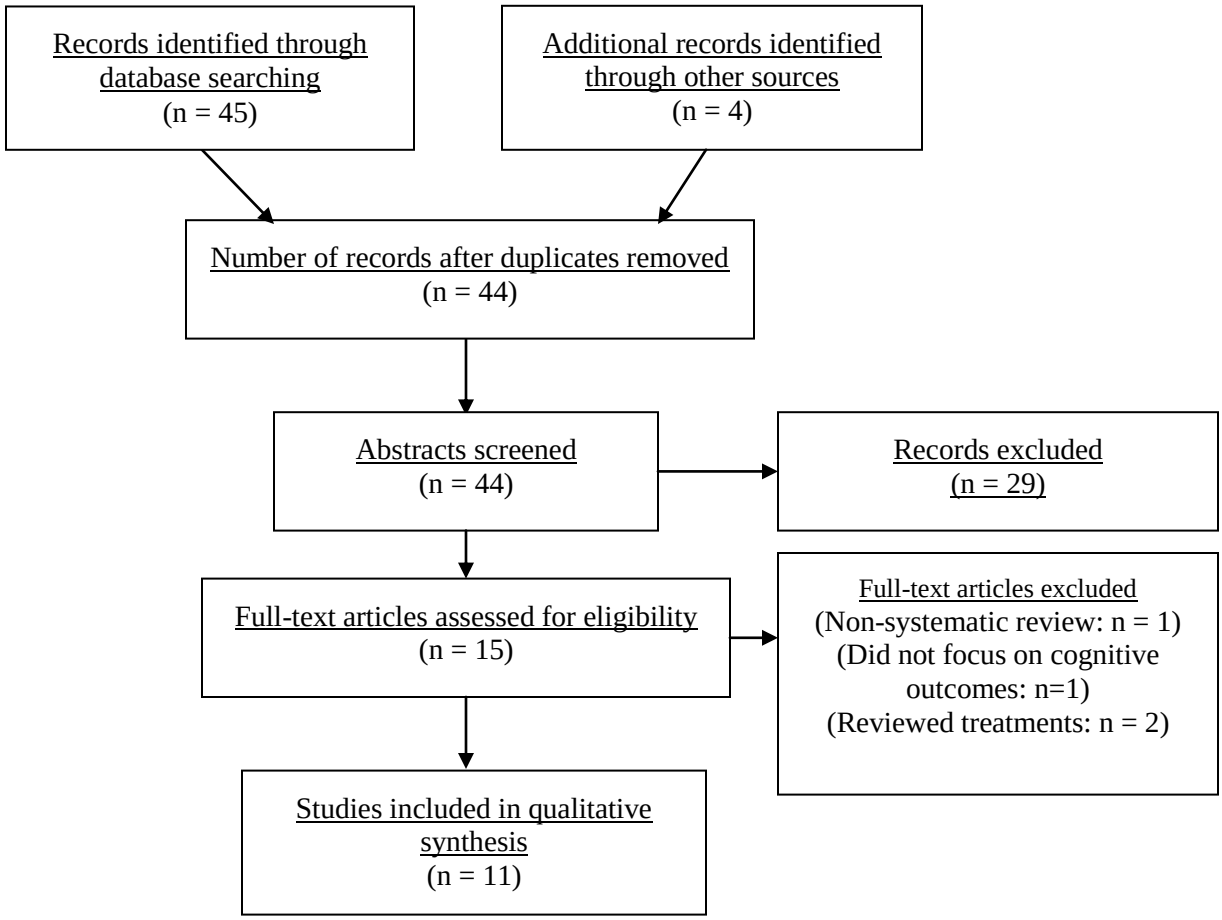

Figure 2. Schematic representation of study inclusion across meta-analyses

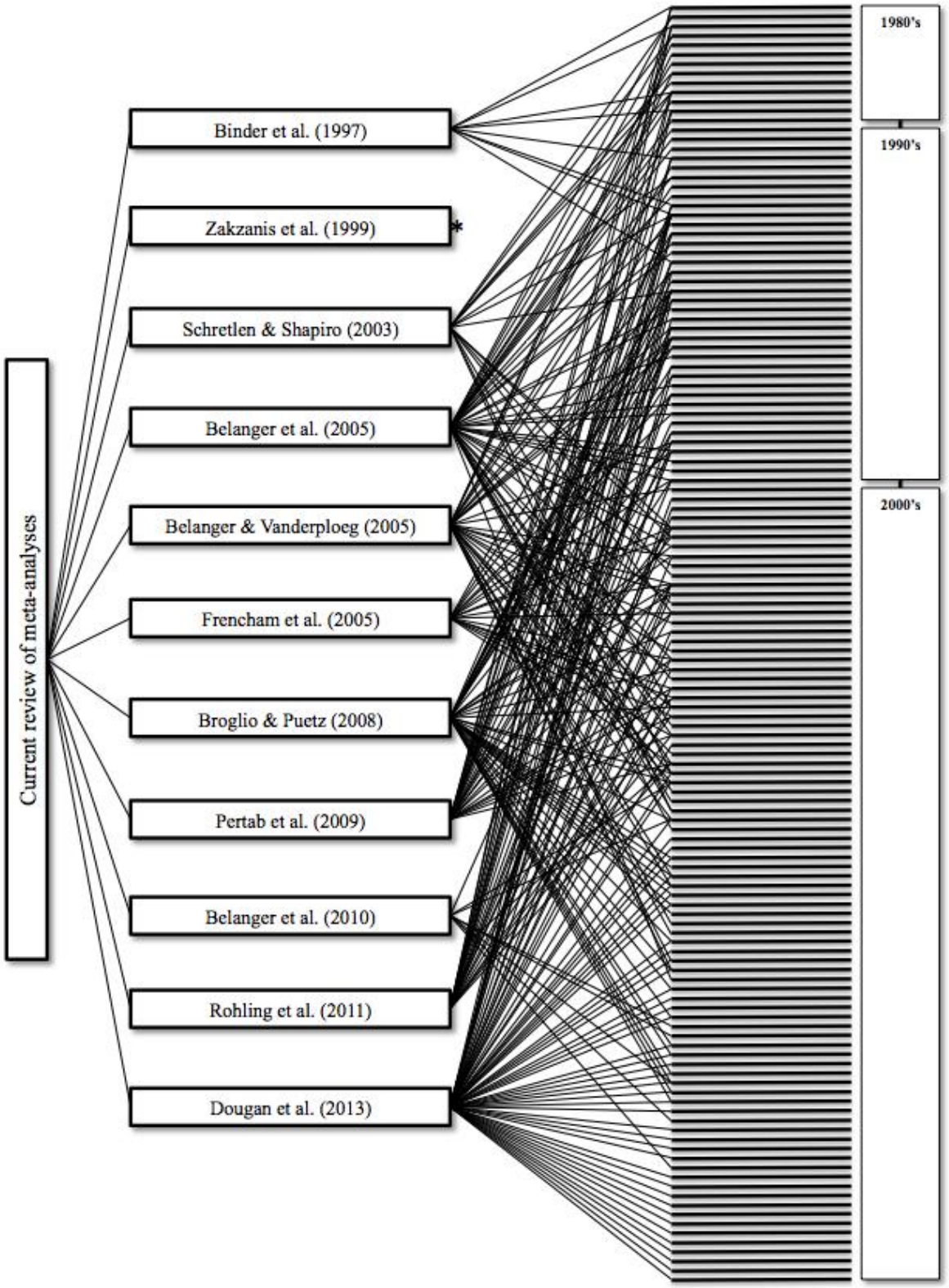

Figure 3. Effect Sizes (*d*) for Primary Outcome Measures with 95% Confidence Intervals

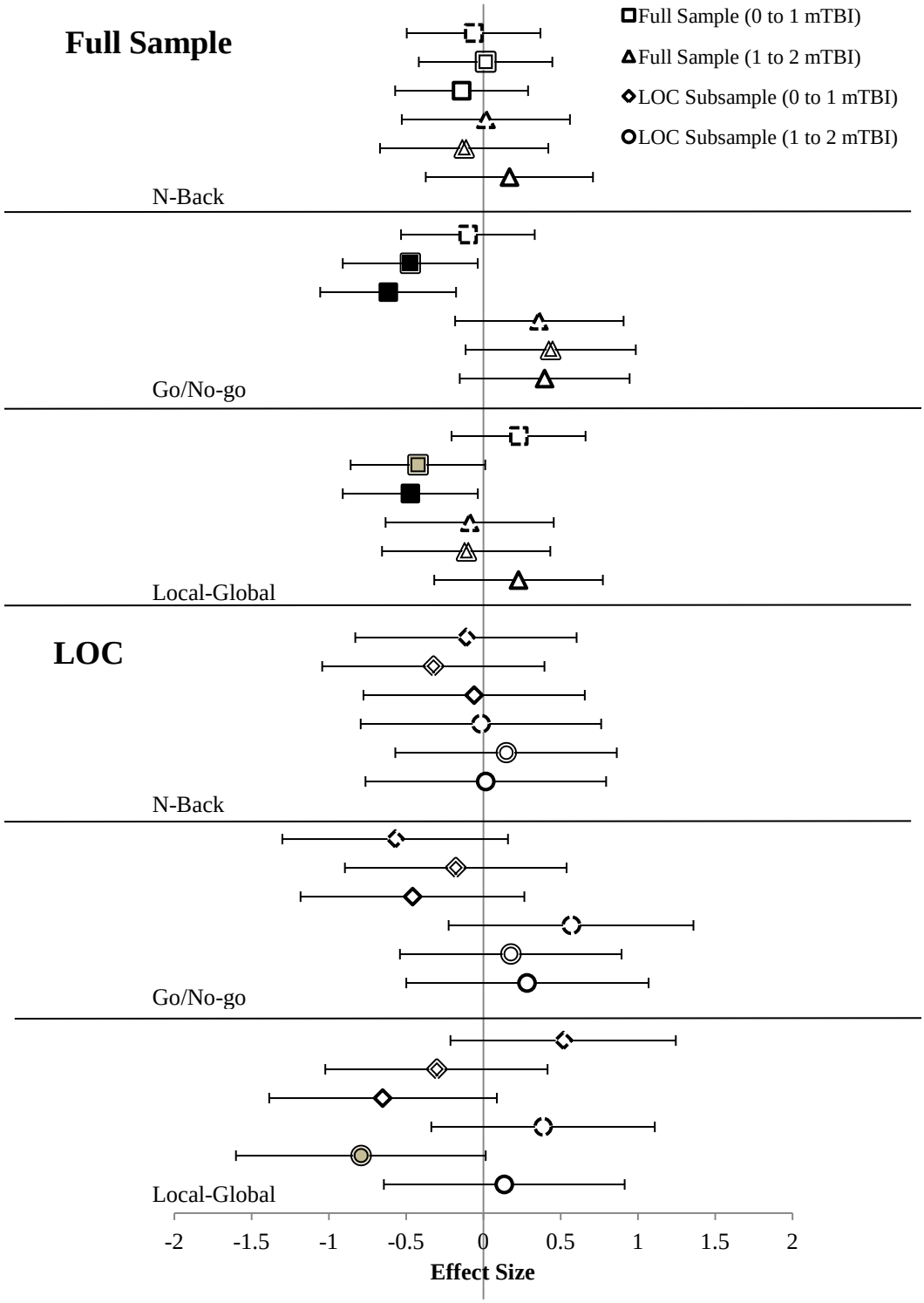

Figure Captions

Figure 1. Graphical representation of the procedure followed during the systematic review.

Figure 2. This diagram represents the levels of data the current study incorporates. Black lines on the right represent 131 studies included across the eleven 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). Appendix A includes the references for all 131 studies. *Zakzanis et al. (1999) did not include a list of studies included specifically in their mTBI meta-analysis, but instead listed studies included in multiple meta-analyses within their full text.

Figure 3. Negative effect sizes indicate worse performance resulting from an increased number of past mTBIs. Dashed marker outlines represent accuracy effect sizes, double-line marker outlines represent mean response time effect sizes, and solid marker outlines represent intra-individual standard deviation effect sizes (All ISD effect sizes derived from the multilevel modeling detrending analysis). Black-filled markers indicate effect sizes with 95% confidence intervals that do not overlap the zero demarcation, whereas grey markers indicate effect sizes that very slightly overlap the zero demarcation (< .02 units). LOC = Loss of Consciousness.

Cited Tables

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 Glascow Coma Scale (13-15), post-traumatic amnesia <24 hours, 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
		To assess how exposure to head injury in sports impacts cognition				(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
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) have 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 two weeks post-injury and at a follow-up assessment	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 post-injury, 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 re-analyze 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. non-symptomatic 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 re-analyze 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) post-injury 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 post-injury assessments, Age, Years of education, Sex, Level of competition, Sports played

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_1/2**	U_G/2**
Binder et al.#	1997	8	314	308			2	*d* = .12 *g* = .07	3.85 3.85	2.00 2.00
Zakzanis et al.	1999	12	952	495	35	64	3	*d* = .61"	19.1	11.79
Schretlen & Shapiro$	2003	15	742	545			4	*d* = .24	7.35	3..99
Belanger & Vanderploeg	2005	21	790	2014			5	*d* = .49	16.50	9.87
		10	264##	176				*d* = .31, *d* = .71^	10.65, 21.50	5.96, 13.69
Belanger et al.	2005	39	1463	1191			7	*d* = .54	16.50	9.87
Frencham et al.	2005	17	634	485	28.46	66.27	4	*g* = .32^^	10.65	5.96
Broglio & Puetz	2008	39	4145+		19.0	92.9	9	*g* = .81^^	23.70	15.54
Pertab et al.#	2009	18	765	583			3	*d* = .45# *g* = .31	16.50 10.65	9.87 5.96
Belanger et al.	2010	8	614 with 2+, 926 with 1				5	*d* = .06	3.85	2.00
Rohling et al.	2011	25	2834	2057	25.5	73.85	2	*d* = .28	10.65	5.96
Dougan et al.	2013	78	3801	5631			8	*d* = .40	13.7	7.93

Note. *AMSTAR study quality ratings ranged from 0 to 11.

**As Cohen (1988) and Grice and Barrett only published U_1 and U_G values for tenth-sized increment increases in *d*, the U_1 and U_G values used in the U_1/2 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).

Binder et al. (1997) and Pertab et al. (2009) reported two effect size statistics: Cohen's *d* and Hedges' *g*. While Pertab et al. used a sample-size bias-correction for *g*, Binder et al. did not correct for sample size.

Represents participants "exposed" to mTBI due to frequent sports-related head contact (e.g., heading in soccer).

^ Exposure meta-analysis produced two effect sizes, based on unexposed control comparison and exposure-cognition correlations, respectively.

$ Meta-analysis involved both mTBI and moderate and severe TBI studies, but *k*, *N*s, and *d* values represent only mTBI-related data.

+ *N* not divided by mTBI and control group, representative of overall sample size.

" Meta-analysis did not report overall effect size, so *d* represents an unweighted average across cognitive domains.

^^ Broglio & 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 Broglio & 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+		.16	.17	.15	

Note. All positive effect sizes denote worse performance resulting from mTBI.

*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.

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 Skill, Verbal, Global, and Motor Ability, respectively.

Table 4. *Summary of Past mTBI Studies Examining IIV*

		Concussion			Control			Study Characteristics			Notable Results
Authors	Year	*N*	$\bar{x}$ Age (*SD*)	Percent Male	*N*	$\bar{x}$ Age (*SD*)	Percent Male	Design	Outcome Measures	IIV Metric	IIV Conclusions
Bleiberg et al.	1997	6	31.83 (3.66)	50.00	6	29.5 (3.73)	50.00	Tested 30 times over 4 days, about 2 days apart. IIV quantified within-day	Procedural RT, running memory, Sternberg, math processing, spatial processing	IQR and Semi-IQR to Median Ratio	Increased IIV on first three tests for TBI group proportionate to slowing mean performance
Burton et al.	2002	19	35.26 (9.72)	78.95	26	32.77 (10.0)	46.15	Ten testing sessions about one week apart	Physical functions (e.g., gait, grip strength, pulse), stress & affect	Res. ISD	Greater right grip strength IIV for concussion, but did not control for mean confounds
Halterman et al.	2006	20	21.00 (1.74)	60.00	20	21.00 (1.81)	60.00	Four testing sessions over one month post-concussion with matched control	Attentional network test: Alerting, orienting and executive function	CV	No IIV differences across groups
Hill & Rohling*	2011	152						Secondary analysis of TBI patient database	Cognitive test battery (Tests not listed)	Dispersion-based ISD	More IIV with increased TBI severity, with concussion having the lowest IIV
Makdissi et al.	2001	6	20.50 (3.10)	100	6	20.30 (4.20)	100	Prospective design with baseline and follow-up within 72 hours of concussion	CogState simple RT	ISD	Decreased IIV for contrordinary least squares at follow-up and increased IIV for concussion group at follow-up proportional to increases in slow RT responses.
MacFlynn et al.	1984	45	30.90 (15.9)	62.22	45	$^{+}$30.90 (15.9)	62.22	Patients tested within 48 hours of concussion, and 6 weeks and 6 months post-injury, compared to matched contrordinary least squares	Four-choice RT test	CV	Greater IIV for concussion patients at first assessment, but no difference by 6 weeks
Rabinowitz & Arnett	2013	71	18.60 (0.80)	21.00	42	18.50 (0.80)	51.00	Athletes tested at baseline and between 0 and 210 days post-concussion (within 1 week on average). Control participants were tested at baseline and 1 month later	Comprehensive Trail-Making, ImPACT, Visuo-spatial Memory Test, Verbal Learning Test, Symbol Digit Modalities, Stroop Color-Word	Dispersion-based ISD	IIV did not increase post-concussion. Athletes with higher baseline IIV trended towards IIV increases post-concussion. IIV correlated with mean performance
Sosnoff et al.	2007	22	19.80 (2.20)	90.91	22	$^{+}$19.80 (2.20)	90.91	Prospective design with baseline and follow-up within 48 hours of concussion	RT, cued RT, visual recognition, animal decoding, and symbol scanning	ISD	No concussion-related IIV differences once controlling for mean RT
Stuss et al.^	1989	22	29.50 (12.6)	68.18	22	27.70 (11.6)	68.18	Compared TBI group IIV at baseline with contrordinary least squares .TBI included concussion group, but also more severe TBI	Simple and multiple choice RT tests	ISD	Greater IIV for head injured group with varying severities, but did not control for mean confounds

Note. *Hill and Rohling (2011) conducted a secondary dispersion analysis of an existing TBI database, with no non-injured control group reported. As well, age and gender composition were not reported. ^Stuss et al. (1989) collapsed all TBI participants into one group for IIV analyses. $^{+}$Denotes estimated mean age and standard deviations, as authors reported using age and gender matched controls. The mTBI demographics listed include only concussed participants, not the additional TBI participants. CV = Coefficient of Variation, IIV = Intra-individual Variability, IQR = Interquartile Range, ISD = Intra-individual Standard Deviation, Res. = Residualized, RT = Reaction Time.

Table 5. *Descriptive Statistics for Task Outcomes based on Number of Past mTBIs*

			N-Back		Local-Global		Go/No-go	
Sample	Number of past mTBIs		*M*	*SD*	*M*	*SD*	*M*	*SD*
Full Sample	0	Accuracy	.693	.243	.868	.182	.975	.089
		MRT	.458	.071	1.55	.390	.339	.055
		ISD (Res.)	10.33	2.99	8.04	3.67	9.08	2.78
		ISD (MLM)	10.10	3.22	8.07	3.71	9.06	2.74
		ISD (Raw)	8.59	2.74	7.32	3.32	7.35	2.20
	1	Accuracy	.678	.235	.902	.105	.968	.045
		MRT	.457	.063	1.75	.544	.369	.071
		ISD (Res.)	10.85	3.01	10.87	7.35	11.01	3.34
		ISD (MLM)	10.53	2.93	10.77	7.19	10.97	3.43
		ISD (Raw)	9.02	2.48	9.78	6.44	8.84	2.69
	2+	Accuracy	.682	.247	.892	.122	.982	.032
		MRT	.467	.095	1.80	.344	.345	.032
		ISD (Res.)	9.59	2.78	9.59	3.34	9.77	2.80
		ISD (MLM)	10.02	2.98	9.49	3.39	9.77	2.56
		ISD (Raw)	8.45	2.51	8.81	2.85	7.86	2.12
LOC Subsample	0	Accuracy	.688	.285	.769	.302	.986	.008
		MRT	.437	.060	1.54	.457	.360	.051
		ISD (Res.)	9.73	3.31	7.26	3.13	9.56	2.73
		ISD (MLM)	9.18	3.59	7.32	3.05	9.48	2.56
		ISD (Raw)	7.86	3.14	6.87	2.68	7.80	2.05
	1	Accuracy	.673	.180	.888	.117	.960	.064
		MRT	.458	.070	1.66	.328	.373	.090
		ISD (Res.)	9.64	3.13	10.71	5.86	10.96	3.64
		ISD (MLM)	9.37	2.80	10.34	5.80	10.96	3.80
		ISD (Raw)	7.94	2.47	9.79	5.08	8.78	3.00
	2+	Accuracy	.669	.319	.921	.030	.986	.009
		MRT	.446	.091	1.92	.329	.352	.044
		ISD (Res.)	8.63	3.19	9.73	3.11	9.66	2.77
		ISD (MLM)	9.32	3.26	9.70	3.23	10.02	2.75
		ISD (Raw)	7.61	2.80	8.99	2.71	7.87	2.05

Note. All Accuracy scores are displayed as percentages from 0 to 1 and all MRT scores are displayed in seconds. ISD = Intra-individual ISD, MLM = Multilevel Modeling, MRT = Mean Response Time, mTBI = mild Traumatic Brain Injury, Res. = Residualized

Table 6. *Correlations between IIV and Mean Performances*

		N-Back			Go/No-go			Local-Global			Other Variables	
		Acc.	MRT	ISD	Acc.	MRT	ISD	Acc.	MRT	ISD	TSI (Mos.)$^{+}$	IPAQ
N-Back	Acc.	1	**-.481****	**-.366****	-.053	-.151	**-.361****	.069	**-.226****	**-.300****	-.024	.064
	MRT	**-.457****	1	**.464****	-.114	**.205***	**.201***	.103	**.240****	**.222***	-.011	-.024
	ISD	-.109	**.438****	1	-.034	.071	**.193***	.016	**.246****	**.290****	.133	-.009
Go/No-go	Acc.	-.052	-.130	-.140	1	**-.668****	.095	-.044	**-.175***	-.116	.076	**.192***
	MRT	-.201	.229	.088	**-.660****	1	**.320****	-.019	**.244****	**.230****	-.157	-.118
	ISD	**-.411****	**.367***	.095	-.115	.309	1	-.036	**.292****	**.307****	-.111	.096
Local-Global	Acc.	.196	.234	.142	-.076	-.013	.129	1	**.243****	-.015	-.044	.036
	MRT	-.036	.264	.167	-.107	.023	.123	**.450****	1	**.858****	-.047	.064
	ISD	-.214	.275	.310	-.223	.201	.207	.221	**.733****	1	.169	.040
Other Variables	TSI (Mos.)$^{+}$	-.149	.298	.207	-.003	-.047	.119	-.183	.063	.394	1	-.038
	IPAQ	.085	.145	-.015	.304	**-.381***	.098	.265	.267	.005	.097	1

Note. Bold values reached significance. The full sample is displayed above the diagonal and the loss of consciousness subsample below the diagonal. $^{+}$TSI correlations involved only participants reporting a past mTBI. ** indicates significance at $p > .01$, * indicates significance at $p > .05$; Acc. = Accuracy, MRT = Mean Response Time, ISD = Intra-individual Standard Deviation, IPAQ = International Physical Activity Questionnaire, TSI (Mos.) = Time Since Injury in Months. All ISD values used in correlation analyses derived from the MLM detrending methodology.

Table 7. *Level-2 Models Results across Executive Constructs*

		N-Back						Local-Global						Go/No-go					
Model Results		Fixed Effects			Random Effects			Fixed Effects			Random Effects			Fixed Effects			Random Effects		
		β	*SE*	*p*	*VC*	*SD*	*p*	*β*	*SE*	*p*	*VC*	*SD*	*p*	*β*	*SE*	*p*	*VC*	*SD*	*p*
Model 1	Intercept	.442	.004	**.000**				1.62	.013	**.000**				.341	.001	**.000**			
	Slope	-.001	.001	.283	.000	.000	.086	000	.000	.929	.000	.002	**.000**	.000	.000	.881	.000	.000	**.000**
	Quadratic	.000	.000	**.000**	.000	.000	**.000**	-.001	.000	**.001**	.000	.000	**.000**	.000	.000	**.000**	.000	.000	**.000**
Model 2	Intercept	.442	.004	**.000**				1.62	.013	**.000**				.341	.001	**.000**			
	Slope	-.001	.001	.091	.000	.000	**.101**	.002	.005	.611	.000	.002	**.001**	.000	.001	.899	.000	.000	**.000**
	Quadratic	.000	.000	**.000**	.000	.000	**.000**	-.001	.000	**.001**	.000	.000	**.000**	.000	.000	**.000**	.000	.000	**.000**
	PA	.000	.000	.275				-.001	.000	.062				.000	.000	.916			
	mTBI	.000	.000	.179				.000	.000	.767				.000	.000	.147			
	PA	.000	.0000	.685				.000	.000	.570				.000	.000	.822			
	mTBI	.000	.000	.728				*.000	.000	**.003**				.000	.000	.380			
Model 3	Intercept	.442	.004	**.000**				1.62	.013	**.000**				.341	.001	**.000**			
	Slope	-.001	.001	.074	.000	.000	.098	.002	.005	.626	.000	.002	**.000**	.000	.000	.918	.000	.000	**.000**
	PA	.000	.000	.184				-.001	.001	.154				.000	.000	.857			
	mTBI	.001	.001	.250				.000	.001	.905				.000	.000	978.			
	PA X mTBI	.000	.000	.446				.000	.000	.818				.000	.000	.600			
	Quadratic	.000	.000	**.000**	.000	.000	**.000**	-.001	.000	**.001**	.000	.000	**.000**	.000	.000	**.000**	.000	.000	**.000**
	PA	.000	.000	.954				.000	.000	.264				.000	.000	.675			
	mTBI	.000	.000	.542				.000	.000	.924				.000	.000	.164			
	PA X mTBI	.000	.000	.599				.000	.000	.243				.000	.000	.241			

Fit Statistics	-2LL (*df*)	Δ-2LL (*p*)	-2LL (*df*)	Δ-2LL (*p*)	-2LL (*df*)	Δ-2LL (*p*)
Model 1	-2809.17 (9)		29877.50 (17)		-23220.63 (11)	
Model 2	-2813.71 (13)	4.54 (>.05)	29864.48 (21)	13.02 (**<.05**)	-23223.70 (15)	-3.07 (>.05)
Model 3	-2814.36 (15)	.65 (>.05)	29863.04 (23)	1.44 (>.05)	-23225.34 (17)	1.64 (>.05)

Note. *The significant *β*-value for mTBI on the local-global quadratic trend was *β* = .000083 prior to rounding. -2LL = -2 Log Likelihood, mTBI = mild Traumatic Brain Injury, PA = Physical Activity Levels, SD = Standard Deviation, SE = Standard Error, VC = Variance Component; Bold characters indicates significance.

Table 8. *Ordinal Logistic Regression Results: N-Back*

Full Sample

	Predictor	β	*SE*	*p*	R^2	ΔR^2
Model 1	Accuracy	-.179	.708	.800	.001	
Model 2	Accuracy	-.235	.825	.776	.001	.000
	Mean RT	-.339	2.87	.906		
Model 3 (Res.)	Accuracy	-.365	.850	.668	.004	.003
	Mean RT	.149	3.10	.960		
	ISD (Res.)	-.036	.067	.584		
Model 3 (MLM)	Accuracy	-.271	.838	.746	.001	.000
	Mean RT	-.602	3.07	.845		
	ISD (MLM)	.000	.067	.998		
Model 3 (Raw)	Accuracy	-.243	.838	.772	.001	.000
	Mean RT	-.474	3.07	.877		
	ISD (Raw)	.005	.075	.952		

Table 9. *Ordinal Logistic Regression Results: Go/No-go*

Full Subsample

	Predictor	β	*SE*	*p*	R^2	ΔR^2
Model 1	Block I Mean RT	2.76	1.97	.161	.016	
Model 2	Block I Mean RT	2.53	3.03	.402	.036	.020
	Block II Accuracy	4.56	3.61	.206		
	Block II Mean RT	4.74	4.70	.313		
Model 3 (Res.)	Block I Mean RT	3.27	3.09	.291	.053	.017
	Block II Accuracy	2.44	3.83	.523		
	Block II Mean RT	.549	5.31	.918		
	Block II ISD (Res.)	.100	.064	.122		
Model 3 (MLM)	Block I Mean RT	3.23	3.08	.295	.053	.017
	Block II Accuracy	2.40	3.78	.525		
	Block II Mean RT	.839	5.26	.873		
	Block II ISD (MLM)	.098	.064	.125		
Model 3 (Raw)	Block I Mean RT	3.22	3.08	.297	.051	.015
	Block II Accuracy	2.48	3.82	.516		
	Block II Mean RT	.948	5.26	.857		
	Block II ISD (Raw)	.117	.080	.146		

Table 10. *Ordinal Logistic Regression Results: Local-Global*

Full Sample

	Predictor	β	*SE*	*p*	R^2	ΔR^2
Model 1	Block I Accuracy	-.455	1.04	.663	.011	
	Block I Mean RT	-.113	.332	.734		
	Block II Accuracy	-.059	1.21	.961		
	Block II Mean RT	-.322	.451	.475		
Model 2	Block I Accuracy	-.711	1.10	.519	.174	.163
	Block I Mean RT	-.279	.417	.503		
	Block II Accuracy	-1.91	1.54	.215		
	Block II Mean RT	-1.29	.781	.098		
	Block III Accuracy	1.46	1.86	.431		
	Block III Mean RT	1.52	.520	**.004**		
Model 3 (Res.)	Block I Accuracy	-1.03	1.14	.369	.243	.069
	Block I Mean RT	-.395	.444	.373		
	Block II Accuracy	-2.07	1.54	.179		
	Block II Mean RT	-1.64	.914	.074		
	Block III Accuracy	.672	1.98	.734		
	Block III Mean RT	2.87	1.19	**.016**		
	Block III ISD (Res.)	-.012	.086	.194		
Model 3 (MLM)	Block I Accuracy	-.920	1.13	.416	.257	.083
	Block I Mean RT	-.415	.458	.365		
	Block II Accuracy	-2.02	1.55	.193		
	Block II Mean RT	-1.71	.999	.088		
	Block III Accuracy	.683	1.96	.728		
	Block III Mean RT	3.13	1.34	**.019**		
	Block III ISD (MLM)	-.135	.097	.166		
Model 3 (Raw)	Block I Accuracy	-.932	1.15	.417	.217	.043
	Block I Mean RT	-.409	.462	.376		
	Block II Accuracy	-1.99	1.57	.204		
	Block II Mean RT	-1.40	.920	.127		
	Block III Accuracy	1.17	1.92	.543		
	Block III Mean RT	2.61	1.19	**.029**		
	Block III ISD (Raw)	-.105	.099	.289		

Note. All Model 3 ΔR^2 values derive from comparisons with Model 2 R^2 values.; ISD = Intra-individual Standard Deviation, LOC = Loss of Consciousness, MLM = Multilevel Modeling, Res. = Residualized, RT = Response Time

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Appendix A

Below is the text used in EBSCOhost literature search for systematic review of reviews, using the following databases: CINAHL, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, MedLine, PsycArticles, and PsycInfo.

(mTBI OR concussion OR mild traumatic brain injury OR mild brain injury OR mild head injury OR minor head injury) AND (neuropsychology OR neuropsychological OR assessment OR cognitive OR cognition) AND (meta-analysis OR systematic review) English; Methodology: -Systematic Review, -Meta Analysis; English Language; Publication Type: Meta Analysis, Systematic Review; Document Type: Cochrane Reviews; English Language; Publication Type: Meta-Analysis, Review; Methodology: -Systematic Review, -Meta Analysis

Appendix B

PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	7-8
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	8
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	9
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	9
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	9
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	9
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8-10
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	11-12
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	11-12

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	29-32
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	65
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	69-71
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	25-27
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	29-32
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	27-29, 32-33
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A