Université de Montréal

Méta-analyse sur les effets cognitifs à long terme des commotions cérébrales chez des athlètes adultes

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Résumé

Contexte théorique : Certaines études suggèrent que les athlètes avec un historique de commotions cérébrales (CC) présentent des symptômes cognitifs à long terme au niveau de la vitesse de traitement de l'information, des fonctions attentionnelles, exécutives et de la mémoire épisodique. Cependant, il existe un manque de consensus sur leur présence.

Méthode : Sept bases de données ont été consultées pour sélectionner des études investiguant l'effet à long terme des CC en comparant des athlètes adultes avec et sans CC, à l'aide de mesures neuropsychologiques. L'évaluation neuropsychologique devait avoir lieu au moins deux mois après la dernière CC.

Résultats : Les lignes directrices de Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) ont été utilisées. La performance des athlètes avec un historique de CC différaient significativement de celle du groupe témoin sur l'encodage d'informations visuelles en mémoire. Cette différence représentait une petite à moyenne taille d'effet (Hedge's $g = -0{,}44$, $p = 0{,}02$). De plus, bien que non significatives, de petites tailles d'effet ont également été trouvées au niveau de l'attention sélective focale et de la génération et la régulation de stratégies. Les tests neuropsychologiques n'ont pas détecté de différences entre les groupes sur les autres domaines cognitifs.

Conclusion : La plupart des athlètes subissant une CC récupèrent généralement rapidement un niveau de fonctionnement cognitif adéquat. Néanmoins, nous ne pouvons pas exclure la possibilité qu'il existe un affaiblissement cognitif à long terme pour une minorité d'individus. Finalement, cette méta-analyse souligne certaines limites méthodologiques de la littérature et oriente les recherches futures pour mieux comprendre les potentiels symptômes cognitifs à long terme.

Mots-clés : Commotions cérébrales d’origine sportive, symptômes cognitifs, long terme, athlètes, neuropsychologie clinique, méta-analyse

Abstract

Background: Research suggests that athletes with a history of concussion (HOC) may present long-term cognitive impairments in processing speed, attention, executive functions (EFs), and episodic memory. However, there is still a lack of consensus regarding the presence of these persisting impairments.

Methods: This study undertook a literature search of seven databases for studies investigating the long-term impact of concussions in college-aged (18–35 years) athletes with a HOC, compared to a control group without a HOC, using neuropsychological measures. The assessment had to be completed at least two months after the last sport-related concussion.

Results: We conducted a meta-analysis according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA). The results support the observation that relative to the control group without HOC, those with HOC are associated with statistically significant, small to medium effect-sized impairment in visual learning memory (Hedge’s g = - 0.44, p = 0.02). Moreover, although not significant, small effect sizes were also found in focal selective attention and EFs strategy generation and regulation. Neuropsychological measures did not detect differences between the groups on the other cognitive domains studied.

Conclusion: It is important to bear in mind that most individuals who sustain sports concussion experience a relatively quick recovery from their injury. Nevertheless, we cannot reject the possibility of long-term cognitive impairment for a minority of athletes with HOC. Thus, this meta-analysis highlights some methodological limitations of the concussion

literature, and as such, directs future research to better understand potential long-term cognitive impairments.

Keywords: Sport-related concussion, cognitive impairments, long-term, athletes, clinical neuropsychology, meta-analysis

Table des matières

Liste des tableaux

Liste des figures

Liste des sigles

AVLT : Auditory-Verbal Learning Test

BVMT (R) : Brief Visuospatial Memory Test (Revised)

CISG : Concussion in Sport Group

COWAT : Controlled Oral Word Association Test

CPTA : Continuous Performance Test of Attention

D-KEFS : Delis—Kaplan Executive Function System

ETC : Encéphalopathie Traumatique Chronique

EFs : Executive functions

ET : Écart-type

FE : Fonctions exécutives

HC : Heathy Controls

HOC : Historic of concussion

HVLT (R) : Hopkins Verbal Learning Test (Revised)

ImPACT : Immediate Post-Concussion Assessment and Cognitive Testing

mTBI : mild Traumatic Brain Injury

PASAT : Paced Auditory Serial Addition Test

PRISMA : Preferred Reporting Items for Systematic Reviews and Meta-analyses

PSU : Penn State Cancellation Test

RAVLT : Rey auditory verbal learning test

RBANS : Repeatable Battery for the Assessment of Neuropsychological Status

RT : Reaction time

RVFT : Regensburger Verbal Fluency Test

SD : Standard deviation

SDMT : Symbol Digit Modalities Test

SMD : standardized mean difference

SRC : Sport-related concussion

TCC léger : Traumatisme craniocérébral léger

TMT-A/B : Trail Making Test A/B

TSI : Time since injury

WHO : World Health Organization Collaborating Centre for Neurotrauma

Liste des abréviations

Adj. : Adjectif

Art. : Article

E.g. : Example, exemple

Etc. : Et cætera

P. : Page

Pour l’amour de la science, pour l’amour de l’humanité.

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Introduction

Au Canada, comme dans de nombreux autres pays, la pratique d'activités sportives fait partie intégrante du mode vie. En effet, le sport s'adresse à toutes les générations, des plus jeunes aux aînés. Chacun peut aussi bien le regarder que le pratiquer et ceux qui le pratiquent peuvent être amateurs ou professionnels. De plus, notre société valorise l'activité physique, considérée comme un vecteur de multiples bénéfices (Powell, Paluch & Blair, 2011).

Or, la pratique sportive n'est pas sans danger, et ce plus particulièrement pour les sports de contact. En effet, un impact direct à la tête ou indirect au corps peut entraîner une blessure au cerveau : c'est la commotion cérébrale (CC). Ce terme que l'on retrouve régulièrement dans les médias a pourtant une définition complexe, qui a évolué au fil du temps et qui provient de diverses sources. L'objectif de cette introduction consiste alors à faire l'état des différentes définitions des traumatismes craniocérébraux légers (TCC légers) et des CC, ainsi que de faire ressortir les principales évolutions qu'elles ont subies au niveau de l'intérêt du sexe biologique, des symptômes éprouvés, des recommandations pour le retour au jeu et des symptômes persistants.

La commotion cérébrale d'origine sportive (CC) est considérée comme un sous-type de TCC léger. De fait il existe une définition pour le TCC léger et une pour la CC. Concernant le TCC léger, *l'American Congress of Rehabilitation Medicine* (ACRM ; Head, 1993) propose des critères diagnostics qui seront repris par la suite, notamment par le *World Health Organization Collaborating Centre for Neurotrauma* (WHO ; von Holst & Cassidy, 2004 ; Kristman & al., 2014) : la perte de connaissance, de moins de 30 minutes, est possible mais non requise ; un état de confusion est observé ; le score au *Glasgow Coma Scale* (GCS) doit être compris entre 13 et 15 ; on note également la présence de déficits neurologiques focaux, transitoires ou non ; et une altération de la mémoire est possible pour les évènements précédents ou suivant immédiatement le choc et qui ne perdure pas plus de 24 heures (Harrington, Malec, Cicerone & Katz, 1993 ; Marshall, Bayley, McCullagh, Velikonja & Berrigan, 2012).

Concernant la CC, c'est en 1997 que l'*American Academy of Neurology* (AAN) propose de définir spécifiquement la CC liée au sport, mais dès 2001 c'est le *Concussion in Sport Group* (CISG) qui s'impose au sein de la communauté scientifique (Aubry & al., 2002). Le dernier regroupement du CISG a eu lieu en 2016 (McCrory & al., 2017) et défini la CC par le résultat de processus pathophysiologiques complexes affectant le cerveau et induits par des forces biomécaniques. La CC peut être causée par un coup direct à la tête ou indirect avec une force impulsive suffisamment puissante pour être transmise à la tête. Dans la plupart des cas, la CC résulte en l'apparition rapide d'altérations des fonctions neurologiques qui se résolvent rapidement et spontanément. Les symptômes en phase aiguë reflètent un dysfonctionnement fonctionnel et non structural, d'où l'absence de résultats positifs en imagerie cérébrale. Les symptômes peuvent inclure ou pas une perte de conscience et la résolution des symptômes suit habituellement un cours séquentiel.

Quand on compare la définition du TCC léger à celle de la CC, on remarque la première fournie des critères diagnostics précis, alors que la 2^{e} est davantage descriptive au regard des différents phénomènes neurophysiologiques. En fait, cette nuance est importante, car l'objectif du CISG est de retirer un athlète du jeu dès qu'une CC est suspectée, et non diagnostiquée (Institut National d'Excellence en Santé et en Services Sociaux (INESS), 2018). Il est pertinent d'avoir proposé cette définition, car seuls les médecins peuvent poser un diagnostic, or il n'y en a pas nécessairement de présents lors des matchs et entraînements sportifs. Il est également important de proposer une définition spécifique aux athlètes, car ils représentent une population qui se distingue de la population générale. En effet, les athlètes risquent de subir plusieurs commotions contrairement aux personnes qui subissent un TCC léger. Le TCC léger apparaît souvent dans un contexte singulier, ayant peu de chance de se reproduire (e.g., accident de la voie publique). L'athlète en revanche qui participe à des compétitions est régulièrement mis à risque de subir des CC. De plus, l'activité physique régulière est connue pour favoriser le fonctionnement cognitif (Fernandes, Arida & Gomez-Pinilla, 2017). Il est donc envisageable que les personnes pratiquant une activité physique régulière présentent un meilleur niveau de fonctionnement cognitif que les personnes sédentaires. Enfin, les athlètes peuvent aussi se distinguer sur le plan psychologique. Ils auraient en effet tendance à prendre des risques significatifs vis-à-vis de leur santé pour atteindre leurs objectifs sportifs (Goldman, Bush & Klatz, 1984 cités par Broshek, De Marco & Freeman, 2015).

Un autre point intéressant est l'évolution de la réflexion autour de l'impact du sexe biologique. En réalité, il faudra attendre 2012 avant que les déclarations ne s'intéressent pour la première fois à cette question pour les CC. C'est donc lors du consensus de Zurich (McCrory & al., 2013) que l'on mentionne, malgré le manque de consensus sur ce point, que les femmes pourraient être plus à risque de subir des CC et que le sexe pourrait également influencer la sévérité de l'accident. Néanmoins plus rien n'est mentionné à ce sujet lors du dernier consensus qui a eu lieu à Berlin (McCrory & al., 2017). L'AMSSM (2019) mentionne quant à elle le besoin de recherche sur l'impact du sexe suite à une CC. En ce qui concerne les TCC légers, c'est en 2013 que l'ANN écrit qu'il est très probable que les femmes soient plus à risque de subir ce type d'accident. En 2018, l'INESS mentionne également qu'être une femme est un facteur de risque pour subir un TCC léger et un facteur de risque de récupération prolongée. Reste qu'à l'heure actuelle la recherche s'est peu penchée sur cette question et que dans le domaine des CC de nombreuses études concernent uniquement les hommes, ce qui limite depuis de nombreuses années la compréhension du rôle du sexe dans les CC.

Indépendamment du sexe, la CC provoque une cascade d'évènements neurométaboliques, neuroélectriques et neurochimiques qui endommagent le cerveau (Ellemberg, 2013). Par exemple, les forces biomécaniques déforment les tissus cérébraux, ce qui comprime les neurones et peut provoquer de la pression intracrânienne. Les CC entraînent également une entrée massive de calcium dans les neurones et une production anormalement élevée d'acide lactique. Ceci perturbe la communication entre les neurones, ce qui peut se traduire par une perte de conscience ou des troubles cognitifs. Enfin, pour se rétablir suite à une CC, le cerveau a besoin de beaucoup d'énergie, alors qu'il en dispose moins qu'à l'habitude. Ce déséquilibre entre les besoins et les réserves disponibles peut engendrer de la fatigue et d'autres symptômes physiques comme les céphalées. L'ensemble de cette crise place la personne dans une position de vulnérabilité importante. Il y a donc plus de risque de subir une nouvelle CC et si un nouvel accident arrive pendant la phase aiguë de la blessure, les conséquences peuvent être mortelles (e.g., syndrome du second impact).

L'ensemble de ces processus pathophysiologiques peut ainsi donner lieu à divers symptômes. L'ACRM (1993) a initialement proposé de les catégoriser en symptômes physiques/somatiques (céphalées, nausées, vomissements, troubles de la vision, de l'audition, de l'équilibre, étourdissement, sensibilité à la lumière ou au bruit) ; symptômes comportementaux et émotionnels (irritabilité, désinhibition, anxiété, dépression) ; et symptômes cognitifs (ralentissement psychomoteur, difficulté de concentration, difficulté de mémorisation). Cette nomenclature est encore souvent utilisé aujourd'hui (Daneshvar, Nowinski, McKee & Cantu, 2011 ; Marshall & al., 2012) et la liste des symptômes possibles suite à un TCC léger ou une CC n'a pas beaucoup changé à travers le temps. Il est tout de même intéressant de noter qu'à l'occasion du consensus de Berlin en 2016 les troubles de l'éveil et de l'équilibre ont été ajoutés à cette liste (McCrory & al., 2017). Plus récemment, l'*American Medical Society for Sports Medicine* (AMSSM ; Harmon & al., 2019) propose une vision plus dynamique de ces symptômes, en prenant en compte les différents chevauchements qui peuvent exister entre eux et donc les différentes raisons qui peuvent sous-tendre un seul et même symptôme (Figure 16).

Établir la liste des symptômes éprouvés par la personne ayant subie une CC, s'avère également importante pour déterminer le moment du retour au jeu. Initialement et durant des décennies, pour les CC il a été recommandé une période de repos physique et cognitive jusqu'à ce que l'athlète soit asymptomatique, ce qui pouvait donc durer plus d'une semaine (AAN, 1997 ; CISG, 2001, 2012 ; et AAN, 2013). Une fois asymptomatique, l'athlète pouvait débuter un protocole de retour au jeu progressif. Ce n'est que récemment, lors du consensus de Berlin (McCrory & al., 2017) que l'on avertit des possibles effets délétères d'une trop grande période de repos (e.g., favorise l'émergence de symptômes dépressifs en raison de l'isolement) et des effets bénéfiques d'une reprise graduelle mais rapide des activités. Ainsi, depuis peu il est recommandé que la période de repos physique et cognitive ne dépasse pas 24 à 48 heures.

Pour terminer, nous allons nous intéresser aux symptômes persistants et à leur définition. Initialement, dans sa définition des TCC légers, l'ACRM (1993) évoque la possibilité de symptômes persistants et nomme cela le syndrome post-commotionnel (SPC), bien qu'elle ne soit pas précise quant à la durée des symptômes. Dans les années qui suivent, alors qu'on aurait pu s'attendre à une définition plus précise du SPC, on note pourtant une absence de référence à de possibles symptômes persistants (AAN, 1997 ; CISG, 2001 ; WHO, 2004 et 2014). Ce n'est qu'en 2012 que le CISG mentionne finalement le fait qu'une minorité d'athlètes (10-15 %) pourrait éprouver des symptômes persistants, ceux-ci étant définis comme durant plus de 10 jours. Lors du dernier regroupement du CISG en 2016, la minorité n'est plus quantifiée et les symptômes persistants sont définis comme durant 10 à 14 jours. En 2013, l'AAN fait référence à de possibles symptômes persistants, mais aucune précision n'est apportée, tout comme l'AMSSM en 2019. Finalement l'INESS (2018) consacre une section aux symptômes à long terme suite à un TCC léger.

Le SPC se caractérise par une constellation de symptômes physiques (maux de tête, vertiges, fatigue, perturbations visuelles, sensibilité au bruit), émotionnels/comportementaux (irritabilité, anxiété, dépression, fatigue) et cognitifs (altération de l'attention, de la mémoire et du jugement) (Ryan & Warden, 2003). Cependant, aujourd'hui, il n'existe toujours pas de consensus autour sa définition (Rose, Fischer, & Heyer, 2015). Les critères mêmes du SPC diffèrent du *Diagnostic and Statistical Manual of Mental Health Disorder*, cinquième édition (DSM-5) à l'*International Classification of Disorders* (ICD-10). En effet, bien que les symptômes soient relativement identiques, selon les critères de l'ICD-10, l'individu doit rapporter au moins 3 symptômes pendant au moins 4 semaines (World Health Organization, 2008), alors que selon le DSM-5, l'individu doit rapporter au moins 3 symptômes pendant au moins 3 mois (American Psychiatric Association, 2013).

En résumé, la CC peut être considérée comme un sous-type de TCC léger. Sur le spectre des TCC, elle serait la forme la moins sévère (Harmon & al., 2019). Il apparaît donc intéressant de considérer leur définition respective comme étant complémentaires, même s'il n'en reste pas moins pertinent de considérer les athlètes comme une population distincte. Par ailleurs nous avons fait état de changements récents dans le champ des CC, notamment sur l'impact du sexe et sur les recommandations quant au retour au jeu. Enfin, le SPC n'est pas une nouvelle notion, mais elle ne cesse de faire débat dans la communauté scientifique. Ainsi, le présent travail a été réalisé dans l'objectif de voir si les CC peuvent induire des symptômes cognitifs persistants. Ce travail pourrait permettre d'accéder à une meilleure compréhension des éventuels effets cognitifs à long terme dus aux CC et ainsi guider les cliniciens dans le choix des tests à administrer lors des évaluations auprès des athlètes avec un historique de CC.

A Meta-analysis on Long-term Cognitive Impact of Sport-related Concussions in College-aged Athletes

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Abstract

Background: Research suggests that athletes with a history of concussion (HOC) may present long-term cognitive impairments in processing speed, attention, executive functions (EFs), and episodic memory. However, there is still a lack of consensus regarding the presence of these persisting impairments. *Methods:* This study undertook a literature search of seven databases for studies investigating the long-term impact of concussions in college-aged (18–35 years) athletes with a HOC, compared to a control group without a HOC, using neuropsychological measures. The assessment had to be completed at least two months after the last sport-related concussion. *Results:* We conducted a meta-analysis according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA). The results support the observation that relative to the control group without HOC, those with HOC are associated with statistically significant, small to medium effect-sized impairment in visual learning memory (Hedge's $g = -0.44$, $p = 0.02$). Moreover, although not significant, small effect sizes were also found in focal selective attention and EFs strategy generation and regulation. Neuropsychological measures did not detect differences between the groups on the other cognitive domains studied. *Conclusion:* It is important to bear in mind that most individuals who sustain sports concussion experience a relatively quick recovery from their injury. Nevertheless, we cannot reject the possibility of long-term cognitive impairment for a minority of athletes with HOC. Thus, this meta-analysis highlights some methodological limitations of the concussion literature, and as such, directs future research to better understand potential long-term cognitive impairments.

Keywords: Sport-related concussion, cognitive impairments, long-term, athletes, clinical neuropsychology, meta-analysis

A Meta-analysis on Long-term Cognitive Impact of Sport-related Concussions in College-aged Athletes

Introduction

Sports concussions are recognized as a public health concern as it is estimated that 3.8 million individuals sustain one each year in the USA (Langlois, Rutland-Brown & Wald, 2006). Moreover, it is a common concern that sports concussions may frequently be underreported or undiagnosed, either because athletes want to avoid being removed from the sporting competition or because they do not recognize that they suffered this injury (Delaney, Caron, Correa & Bloom, 2018; Delaney, Lamfookon, Bloom, Al-Kashmiri & Correa, 2015; McCrea, Hammeke, Olsen, Leo & Guskiewicz, 2004; Meehan III, Mannix, Stracciolini, Elbin & Collins, 2013). The last consensus statement on concussions in sports defined it as a mild traumatic brain injury (mTBI) by which biomechanical forces induce complex pathophysiological processes that affect the brain. The impact can either be direct or indirect, and results in the alteration of mental status, whether this is accompanied by a loss of consciousness or not (McCrory & al., 2017). This statement is supported by many studies that suggest that symptoms are short-lived and that most athletes fully recover from their injury within two to three weeks (Harmon & al., 2013; Pontifex, O'connor, Broglio & Hillman, 2009). This likely explains why studies on the long-term outcome following sports concussion have been few and far between and that they have mainly been interested in post-concussion syndrome and retired athletes (Hiploylee & al., 2017; Manley & al., 2017).

The long-term consequences of sports concussion in seemingly healthy and active athletes who sustained one or more concussion have become a topic of debate (Ellemberg, 2009; FeDen, 2016; Solomon, Ott, & Lovell, 2011). Although there is accumulating evidence of persisting cognitive impairments following a sports concussion, contradictory findings in the literature likely contribute to the lack of consensus on the issue. However, these contradictory findings could depend on methodological issues, the cognitive domain assessed or the tests used.

Although a majority of studies suggest that athletes seem to be fully recovered in most cognitive domains, there is accumulating evidence for some long-term cognitive differences between athletes with and without a history of concussion (HOC; one or more concussion) in processing speed, attention, executive functions, and episodic memory. Processing speed is a measure of efficiency on relatively simple cognitive operations (Sweet, 2011). Athletes with a HOC could have long-term cognitive impairment on this domain. For example, Terry et al. (2012) reported a group difference between athletes with a HOC and controls on the attention index from the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), which is considered to be a measure of processing speed. Nevertheless, Killam, Cautin et Santucci (2005) did not find any difference between athletes with a HOC and controls on this same measure. Regarding methodological differences between these two studies, on the one hand, Terry et al. (2012) only assessed males with multiple concussions and time since injury (TSI) was very heterogeneous. On the other hand, Killam et al. (2005) recruited both male and female participants with one or more concussions, and separated athletes with recent and non-recent sports concussion. Other studies assessing athletes who had either one or more concussion on processing speed with different tests (Symbol Digit Modalities Test (SDMT); Symbol match; Trail Making Test-A (TMT-A)) did not find any group difference (Thornton, Cox, Whitfield & Fouladi, 2008; Wall & al., 2006). In addition, the SDMT does not seem to be able to pick up long-term differences, contrary to the RBANS (Terry & al., 2012). Thus, the different tests that are administered to athletes can also explain contradictory results.

Regarding attention, which underlays each and every one of our cognitive functions, athletes could also exhibit long-term cognitive impairments on this domain. For example, Moore, Lepine et Ellemberg (2017) found group differences in reaction time during an Oddball task, whereas, Baillargeon, Lassonde, Leclerc et Ellemberg (2012) did not. Theses studies are quite comparable, except with regards to TSI which is quite heterogeneous (27+/-3 months) for Moore et al. (2017), contrary to Baillargeon et al. (2012) where TSI was narrower (6+/-3 months). The number of previously sustained concussions is also quite variable. In fact, the first study assessed athletes with one, two or three concussions, whereas the second chose athletes with one or two concussions. These methodological differences could have contributed to the contradictory results. Further, none of the studies that used clinical standardized tests of attention report long-term impaired cognitive performance (Ellemberg, Leclerc, Couture & Daigle, 2007; Matser, Kessels, Lezak, Jordan & Troost, 1999; Sicard, Moore & Ellemberg, 2018). It is possible that this can be explained by the fact that each study used a different test to measure attention (Ruff 2&7; Brief test of Attention ; Bourdon-Wiserma test; Cogstate), and that TSI and the number of previously incurred concussions varied greatly from one study to the other.

Executive functions (EFs) refer to a family of top-down mental processes that allow us to plan actions to achieve a specific goal, to adapt to a given situation, to self-regulate actions, and to self-correct in case of error (Diamond, 2013). Studies seem to show that athletes with a HOC differed from athletes without a HOC, especially in working memory, which is a sub-function of executive functions (EFs) (Sicard, Moore & Ellemberg, 2018 and 2017; Terry & al., 2012; Thornton & al., 2008). Nevertheless, we also find inconsistent results for other sub-functions of EFs. For example, Kemp, Duff et Hampson (2016) and McCrea et al. (2003) both assessed college-aged athletes with the Controlled Oral Word Association Test (COWAT), but the first group did not report difference whilst the other has. Note that in these longitudinal studies, Kemp et al. (2016) enrolled athletes with one or more concussion and reassessed them five years after the baseline, whereas McCrea et al. (2003) reassessed athletes with a single concussion at 90 days post-concussion.

Finally, episodic memory allows us to learn, remember and retrieve information (Tulving, 1995). Performances on this domain seem to frequently differ between athletes with and without a HOC, but there are also contradictory findings. For example, regarding the ability to learn a list of words in five trials, Kemp et al. (2016) found group differences, whereas Ellemberg et al. (2007) did not. Kemp al. (2016) assessed males with one or more concussions five years after the baseline and Ellemberg et al. (2007) assessed females approximately six months following their first concussion. In another study assessing verbal learning in both male and female, a group difference emerged (Killam & al., 2005). Matser et al. (1999) also found group differences assessing both visual and verbal encoding. Regarding the delay recall, using the Hopkins Verbal Learning Test (HVLT), Moore et al. (2017) and McCrea et al. (2003) did not find differences on the number of words recall. Nevertheless, Moore et al. (2017) added another dependent variable, which was the total number of errors made during this recall, and group difference emerged on this outcome. Regarding both visual and verbal delay recall, Killam et al. (2005) found differences and Baillargeon et al. (2012) did not. Killam et al. (2005) assessed both males and females after several months to several years with the RBANS, whereas Baillargeon et al. (2012) assessed males after approximately six months post concussion with the Brief Visuospatial Memory Test (BVMT) and the HVLT.

Although sparse, these results do provide some support for long-term cognitive impairments in athletes with a HOC. This is also consistent with the growing body of evidence suggesting that retired athletes with a HOC are at heightened risk of developing neurodegenerative diseases (Chatterjee & al., 2015; Guskiewicz & al., 2005; Perry & al., 2016).

Meta-analyses are particularly useful when there are contradictory results in the literature. In the present case, a meta-analysis could provide the necessary power to detect potential cognitive differences and allow us to appreciate the magnitude of the effects (Borenstein, Hedges, Higgins, & Rothstein, 2011). To the best of our knowledge, only one meta-analysis was completed to determine the magnitude of long-term cognitive impairments in athletes with multiple concussions across multiple cognitive domains (Belanger, Spiegel &Vanderploeg, 2010). Their results show a significant small effect size on the retrieval phase of episodic memory (delay visual and verbal recalls) and a significant small effect size in executive functions (strategy generation and regulation; set-shifting and interference management). A small effect size in learning was also reported, though it was not significant. Although this study brings some support to the hypothesis of persisting impaired cognitive performances following a sports concussion, some limitations also need to be taken into consideration. First, the authors only included studies for which athletes with a history of multiple concussions were compared to controls who were athletes who sustained a single concussion. Given that some studies suggest the presence of subtle long-term cognitive impairments after sustaining a single concussion, it might be preferable for controls not to have a history of concussion (Ellemberg & al., 2007; Moore, Broglio & Hillman, 2014). In addition, the theoretical construct of executive functions was not divided into sub-functions but evaluated as a single cognitive domain. Moreover, because some studies report results from several tests that assess the same cognitive domain, the authors decided to take the means from all measures assessing the same cognitive domain. Furthermore, they obtained significant measures of heterogeneity (using the Q statistic) across most of the cognitive domains, which generally does not allow the summary effect to be accurately interpreted. Note that this heterogeneity could indicate that the outcome measures combined in the forest plot might not well represent a given cognitive domain. Finally, since their meta-analysis, which ended in 2009, additional studies on long-term cognitive symptoms have been published and need to be taken into consideration.

Therefore, our objective was to investigate long-term cognitive performances, in college-aged athletes with one or more concussions compared to controls without a history of concussion. This could lead to a better understanding of potential adverse effects stemming from sports concussions and guide clinicians in the cognitive assessment of athletes with a HOC.

Methods

The guidelines for Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) were followed to complete the present meta-analysis (Moher, Liberati, Tetzlaff & Altman, 2009).

Inclusion/exclusion criteria

To ensure a reasonably homogenous set of studies and to allow for the calculation of effect sizes pertaining to the potential long-term cognitive impairments related to the HOC, studies had to meet the following criteria to be included in the analysis:

1) Participants had to be professional or non-professional athletes aged from 18 to 35 years. Only young adults were included to avoid the effects of development or aging on cognitive performance;

2) Medically diagnosed or self-reported concussions had to occur from 18 years of age (Meehan, Mirdamadi, Martini & Broglio, 2017) to investigate the effects of concussion during adulthood. Participants could have a history of one or more concussions;

3) Time since injury had to be at least two months post-concussion to allow the investigation of long-term effects. Currently, there is no consensus as to the minimum time post-concussion required for an athlete to be considered as presenting long-terming neuropsychological impairments. The Berlin consensus statement on concussions in sport (McCrory & al., 2017) defines post-concussive symptoms in adults as persisting beyond 14 days. However, the *Institut national d'excellence en santé et en services sociaux* (INESSS, 2018) considers that symptoms are persisting when present over three months. Note that the authors have considered mTBI not only related to sport. Considering these two time frames, we chose to be close to the INESS definition to be conservative regarding the potential long-term impact. But we also wanted to be inclusive regarding the literature, considering the fact that there are some studies investigating the long-term impact of sports concussions two months after the last concussion;

4) Studies including athletes with a history of neurodevelopmental, neurological or psychiatric disorders prior to their first sports concussion were excluded;

5) Athletes with a HOC had to be compared to a control group without concussion;

6) Neuropsychological measures could include standardized clinical tests, screening tests or experimental tasks. This allows us to study the tools used in clinical and research settings;

7) Only studies reporting means and standard deviations were included to allow us to calculate effect sizes;

8) Studies had to be conducted according to an experimental paradigm (cross-sectional or longitudinal); in the case of longitudinal study, we focus our interest on the outcomes obtained in respect to our time criterion. Case studies were not included.

Search Strategies

Researcher FR first conducted a formal search under the supervision of a university librarian on April 18, 2017. The following databases were consulted: Embase, Pubmed, PsychInfo, Sport Discuss, Web of science, and Cochrane. The search was limited to studies from 1880 to 2017, published in English and French. The keywords correspond to three concepts: HOC, neuropsychology, and athletes. For the three concepts, the keywords were combined with each other by "AND". Within a given concept, the keywords were separated by "OR". Descriptors were also used when available. 1) HOC: “heading” OR “head injury” OR “head injuries” OR “head injured” OR “brain injury” OR “brain injuries” OR “brain injured” OR “trauma” OR “traumatic brain injury” OR “repetitive mild traumatic brain injury” OR “mild brain injury” OR “sports-related head injury” OR “concuss*” AND 2)

Neuropsychology : “neuropsycholog*” OR “cogniti*” OR “neurocogniti*” OR “deficits” OR “outcome assessment” OR “Executive Control” OR “Executive Function” OR “Attention” OR “Memory” OR “Problem Solving” OR “Decision-Making” OR “Inhibition” OR “Working memory” OR “Shifting” OR “Switch” AND 3) Athletes: “Atlhlet*” OR “Sport*”. Once all records were downloading, FR removed duplicates.

In addition to the formal data collection, a second researcher, GC, conducted an informal search. By informal, we mean that the researcher did not proceed with a concept map and predefined keywords. He adopted an experiential approach, collecting data based on the objective of the present study and the inclusion/exclusion criteria (see appendix A). This informal search was conducted between May 13, 2017 and June 5, 2017 on five databases (Embase, Google scholar, Pubmed, Scopus, and Web of science) with the three same concepts of HOC, neuropsychology, and athletes. GC removed duplicates each time he finishes downloading records from one database and at the end of his total search. In addition, GC examined the reference sections of systematic reviews and meta-analysis that were carried out on the general topic of concussion to minimize the possibility of overlooking studies missed in the database searches. In other words, systematic reviews and meta-analysis were a way to add references but they were not included in the statistical analysis of this study. GC also looked in the gray literature (for example, studies under publication, theses, etc.) and conducted a manual search in the bibliography of studies included in the analysis. We combined these two search strategies (formal and informal) because the rigidity of the formal process can lead to some oversights. To the best of our knowledge, this is the first time this type of informal procedure has been used in a meta-analytic review.

Data Extraction

During the data collection process, both FR and GC collected records on Endnote and sorted them into ‘accepted’ or ‘excluded’ groups based on title and summary. To double-check this first sorting, DE, a third researcher, verified each data set. No modification was made and records from FR and GC were pooled together, thus the formal and informal searches ended here.

For eligibility, we wanted FR and GC to proceed independently to control for attentional errors that could occur during data extraction and to minimize the effect of subjectivity in classifying outcomes. Thus, we needed to create a systematic procedure to extract data from studies. Consequently, a first pilot sorting for eligibility was conducted by FR to create a data table and an extraction guide, which helps fulfill the table with the same codes and categorize the cognitive outcomes in the same way (see the section *cognitive outcome measures* for details).

The final table listed rejected studies (with the reasons for rejection) and the potentially accepted studies. The sociodemographic data for athletes with a HOC and their controls (number of participants, percentage of males, mean age, athletes or non-athletes) were extracted for the potentially accepted studies. For the experimental group, we extracted data relative to the HOC (i.e., mean number of sports concussions, time since injury, type of diagnosis) and the neuropsychological tests that were used (i.e., type of tests, test name and measures, cognitive domains (and subdomains), raw scores, *p* values). In studies with more than one HOC group, a consensus was reached to extract data from one group. This could introduce bias, but it is the only way to avoid transforming original data. Regarding missing data, we intended to contact authors of the primary studies.

FR and GC then met to review the content of their tables, including the reason for the exclusion and the data to be extracted for the potentially selected studies. Whenever there was a disagreement, a third researcher, DE, was consulted.

Cognitive Outcome Measures

The outcome measures were the scores on neuropsychological tests for athletes with a HOC and their controls. First, these tests were categorized into standardized clinical tests, screening tests, or experimental tasks. On one side, clinical and screening tests are both psychometric tools (qualifying the performance of a person according to the norms' test), used in clinical settings and can be paper-pencil or computerized tasks. The difference between these two types of tests concerns the objective of the assessment. In fact, the screening test is designed to give a global, rapid and superficial overview of several cognitive functions. However, the clinical test is more function-specific and is not self-sufficient: it only makes sense in a thorough neuropsychological evaluation. On the other side, experimental task is often creating for research purpose and therefore do not imply to be standardized (comparing the study group differences). It is often function-specific, often computerized and often longer than clinical or screening tests.

Then, based on contemporary models of cognitive functioning outcomes were sorted into four cognitive domains: processing speed, attention, executive functions, and episodic memory. This allowed us to generate a forest plot representing cognitive domains.

We chose Van Zomeren and Brouwer's model of attention (1994) because it distinguishes attentional components that are usually assessed by neuropsychological tests: focal selective attention and sustained attention. For the episodic memory, Tulving's model

(1995) was chosen. This model describes three stages of the memory processes (encoding, storage, and retrieval), which are directly addressed in neuropsychological tests of memory. As for the executive functions (EFs), we retained the model of Testa, Bennett et Ponsford (2012) for two main reasons. First, their goal is to operationalize EFs for neuropsychological assessment, and second, this model was used by Stephan et al. (2017) in their meta-analysis where effect sizes were calculated by neuropsychological measures and where summary effects represent cognitive domains. According to Testa's model, there are six sub-executive functions: prospective working memory; strategy generation and regulation; set-shifting and interference management; task analysis; response inhibition; self-monitoring; and self-maintenance. Finally, no relevant model of processing speed was found, mostly because it is part of every cognitive process. Nevertheless, it was considered as a cognitive domain to be consistent with other reviews and meta-analysis and because some authors find long-term impaired performance in processing speed following a concussion (Ellemberg & al., 2007). The classification based on the above-mentioned models lead to the creation of eight subcategories (see Table 1).

Assessment of the Risk of Bias

Randomized control trials are seldom conducted in sports concussion research and guidelines for the assessment of risk of bias for non-randomized control trials do not exist. Thus, we established the following quality criteria to assess the risk of bias:

1) Which experimental design was used (e.g., cross-sectional, longitudinal)?

2) Which definition of sports concussion was used?

3) Were neurodevelopmental disorders part of the exclusion criteria?

4) Under which conditions participants were assessed (individual or group assessment)?

5) Was age, sex, and years of education controlled for? Were there other controlled variables?

According to the answers to these questions, quality points (from zero to three stars) were attributed to the study, but we did not establish a cut-off score. The quality points were useful to make comparisons between studies and to start discussion around their quality. Then, a meeting with FR, GC, and DE was organized to homogenize of the final sample of potentially included studies to improve the global quality of this meta-analysis.

We counter-verified the results of our risk assessment procedure with the Newcastel—Ottawa Quality Assessment Scale for Cohort Studies (Wells & al., 2014). This scale assesses the quality over three domains: selection, comparability, and outcome. A star system is used to have a semi-quantitative assessment, with a greater number of stars (maximum of 9) indicating higher quality of the study. There is no cut-of available.

Data Analysis

Some studies report results from several tests that assess the same cognitive domain. To respect the assumption of independence of scores in statistical analysis, we decided to use only one measure from a given cognitive domain for each study. Taking the means from all measures assessing the same cognitive domain could confound subtle differences between the tests. To choose the appropriate outcome for each study, we used theoretical and sample-related cues. Regarding theoretical models, we tried to choose the most appropriate measure to assess a given cognitive domain. Regarding the sample-related cues, we try to choose measures that were the most frequently used in the different studies of this meta-analysis, in the interests of statistical homogeneity. These indices were not used in a systematic way, but according to the unique characteristics of the forest plot to be generated. Different analyzes were performed according to the type of task (screening tests, standard clinical tests and experimental tasks).

Results were analyzed using Review Manager 5.3 (RevMan 5.3) with an alpha risk of 5% for all (sub)domains with a minimum of two neuropsychological measures required for each cognitive domain (Goodall & al., 2018). We used the random effects model because of heterogeneity across studies. The standardized mean difference (SMD) was calculated using Hedges' adjusted g with 95% confidence intervals due to the heterogeneity of neuropsychological measures used within domains. Between-study heterogeneity of effect sizes was assessed using the I^2 and the τ^2 statistics. I^2, which is more intuitive, indicates the magnitude (in percentage) of between-study variability due to factors such as participant or methodological differences rather than chance alone. I^2 values of 25%, 50%, and 75%, respectively indicate small, moderate, and high heterogeneity (Borenstein & al., 2011). Measurement scales were standardized so that lower scores were representative of poorer cognitive functioning. To respect that, for processing speed where a lower score indicated a greater performance we had to transform positive values in negative values. For the purpose of this study, participants were classified as cognitively impaired if their outcome measure score significantly differed from that of the control group.

Regarding the publication bias, we chose not to perform a statistical test to control for it. Indeed, some authors emphasize the problem of subjectivity in the interpretation of the funnel plot and advise against doing it when there are fewer than 10 studies (Sterne & al., 2011; Terrin, Schmid & Lau, 2005). It is through the combination of formal and informal research strategies, as well as research in gray literature that we minimized the publication bias as much as possible.

Results

Study selection

The formal electronic search (FR) identified 3,014 studies (2,305 duplicates removed) and the informal search (GC) identified 2,876 studies (794 duplicates removed), resulting in 5,890 studies screened. Of these, 5,374 studies were excluded based on the title and abstract alone (n = 516).

Of these 516 studies, 13% (66 references) were duplicates from both search strategies, suggesting that combining the two research strategies was valuable. This resulted in 450 full articles that were screened. Fifty-nine studies (14%) were excluded based on age criteria. A hundred and seventy-five studies (42%) were excluded because they did not assess athletes with a HOC (e.g., investigate traumatic brain injury due to motor vehicle accident). Thirty-six studies (8%) were excluded because they did not pertain to the consequences of a HOC (e.g., investigate sub concussion's consequences). Five studies (1%) were excluded because the concussions were sustained before the age of 18 years. Fifty-nine studies (14%) were excluded based on the TSI exclusion criteria. Twenty-one studies (5%) were excluded because TSI was not specified. Fifteen studies (3%) were excluded because they did not use neuropsychological tests. Eighteen studies (4%) were excluded because they were not experimental studies (e.g., critical reviews). Twenty studies (5%) were excluded because of a lack of quality (mostly because of the presence of HOC in the control group). Finally, sixteen studies (4%) were excluded because of other reasons (e.g., intervention studies; see appendix C, p. 74). Therefore, following this data extraction process, 28 studies had the potential to be included in analysis.

Additional studies were excluded to homogenize the final sample. Because at this stage of the process most studies including only males, studies that including only females or a minority of males were excluded, even if this was not part of our primary exclusion criterion (n = 5). One study was rejected because it was the only one with a control group formed of non-athletes. Two studies with sample sizes of less than ten were excluded too. Finally, two additional studies were excluded because we suspected that the sports concussion occurred before 18 years. Thus, our final sample included 18 studies, all with a cross-sectional design (see Fig. 2, p. 62 and appendix B, p. 71).

Study Characteristics

The sample sizes for the healthy controls was 1,242 (82% males) and 421 (89% males) for athletes with a HOC. The mean age for healthy controls was 20.09 years (SD = 1.79) and it was 21.39 years (SD = 1.96) for those with a HOC. Athletes from the HOC group had a mean number of 2.62 (SD = 1.74) concussions. Note that for two studies, there was more than one HOC group, based on the number of previous concussions (Bruce et Echemendia, study A and B, 2009 ; De Beaumont, Brisson, Lassonde & Jolicoeur, 2007). We decided to extract data from groups made of athletes with multiple concussions. Even if it also introduces a bias, we made the decision in the interests of homogeneity. In fact, none of the eighteen studies selected had athletes who suffered only a single concussion. Finally, the TSI ranged from 5.27 to 49.85 months (M = 22.56, SD = 22.29).

A few studies did not report certain characteristics of the sample and we did not obtain responses from the authors regarding this missing information. Because the missing information was few, the studies were not excluded from the statistical analysis. This is how we decided to treat the problematic variables: Bruce et Echemendia (study A and B, 2009) do not provide mean and standard deviation for TSI, but these two studies have a total weight of 20%, which is not negligible. Therefore, we decided to recomputed a weight per study while ignoring Bruce et Echemendia (2009) to obtain the global mean and standard deviation for the TSI. Moreover, Singh et al. (2014) did not provide the mean number of concussions, and Thoma et al. (2015) did not provide the specific percentage of males. Because their weight were respectively 6%, we ignored the missing data (not comprised it into the calculation of global mean number of concussions and global percentage of males) without recalculating each study weight. Details for each study are given in Table 2.

Assessment of Risk of Bias

According to our 3-point scale system, of the 18 total studies included, only 22% had one point, 39% had two points and also 39% had the maximum of three points, which is satisfactory. According to the Newcastel—Ottawa Quality Assessment Scale for Cohort Studies (Wells & al. 2014), the overall methodological quality of the included studies was good, with an average of 7.80 (SD =1.04) on a maximum of nine points (range = 6–9). This score confirms that quality criteria were defined appropriately. Because of this, we chose to keep all the studies that have been already selected for the statistical analysis.

Cognitive functioning

Summary of scores from meta-analysis of cognitive domains are provided in Table 3.

Processing speed

Clinical tests

In most studies, processing speed was assessed by Symbol Digit Modalities Tests (SDMT) (see Fig. 2). Outcome measures were found to be appropriately homogenous, $\tau^2 = 0.02$, df (9), $p = 0.29$; $I^2 = 17\%$. No significant group effect on performance was observed, Hedge's g = -0.12, z = 0.95, $p = 0.34$.

Screening Tests

Processing speed assessed by ImPACT—motor speed did not violate assumptions of homogeneity, $\tau^2 = 0.00$, df (4), $p = 0.36$; $I^2 = 9\%$. Performance across groups were not found to have a significant difference, Hedge's g = 0.10, z = 1.03, $p = 0.30$ (see Fig. 3).

Focal selective attention

Clinical tests

In most studies, focal selective attention was assessed by the Penn State Cancellation Test (PSU) and outcome measures were found to be appropriately homogenous, $\tau^2 = 0.00$, df (5), $p = 0.98$; $I^2 = 0\%$. Performance across groups were not found to have a significant difference, Hedge's g = -0.23, z = 1.44, $p = 0.15$. However, we can observe that the summary effect visually tends to indicate that athletes with a HOC have a lower score relative to controls (see Fig. 4). A tendency is defined by an effect size that is close or equal to a small effect size, but which is not significant.

Experimental Tasks

In most studies, focal selective attention was assessed by oddball tasks and outcome measures did not violate assumptions of homogeneity, $\tau^2 = 0.02$, df (4), $p = 0.28$; $I^2 = 21\%$. Performance across groups were not found to have a significant difference, Hedge's g = -0.07, z = 0.51, $p = 0.61$ (see Fig. 5).

EFs—strategy generation and regulation

Clinical tests

In most studies, strategy generation and regulation was assessed by verbal fluency tests (see Fig. 6). Outcome measures were found to be appropriately homogenous, $\tau^2 = 0.04$, df (9), $p = 0.20$; $I^2 = 26\%$. Even if there is a tendency for athletes with a HOC to perform worse, performance across groups was not significantly different, Hedge's g = -0.20, z = 1.56, $p =$ 0.12. Nevertheless, when we consider individual studies, the two studies with the largest effect sizes are different from others because their confidence intervals do not cross the central bar. Thus, athletes with a HOC performed worse than controls on the letter version of the verbal fluency tests used in the studies of Wilke et al. (2017) and List, Ott, Bukowski, Lindenberg et Floel (2015).

EFs—set-shifting and interference management

Clinical tests

Different clinical tests were used to assess set-shifting and interference management (see Fig. 7). There was a significantly moderate heterogeneity between studies, $\tau^2 = 0.13$, df (9), $p = 0.03$; $I^2 = 52\%$. In fact, we can see that the two studies with largest effect sizes are different from others because their confidence intervals did not cross the central bar. The effect size obtained by the letter-switching condition of the List et al. (2015) and Wilke et al. (2017) studies, show that athletes with a HOC performed worse than controls. However, regarding the summary effect, no significant group effect on performance was observed in set-shifting and interference management, Hedge's g = -0.17, z = 1.05, *p* = 0.29. Nevertheless, we observe a tendency for athletes with a HOC to have a lower performance relative to controls.

Experimental Tasks

Measures for set-shifting and interference management assessed by experimental tasks were pooled (see Fig. 8). Outcome measures did not violate assumptions of homogeneity, τ^2 = 0.00, df (1), $p = 0.88$; $I^2 = 0\%$. No significant group difference was observed, Hedge's g = 0.50, z = 1.84, $p = 0.07$.

EFs—response inhibition

Screening tests

Three measures were pooled to assess response inhibition (see Fig. 9). All measures came from the same screening tests but analysis of τ^2 and I^2 revealed a significantly high heterogeneity between studies, $\tau^2 = 0.38$, df (2), $p < 0.001$; $I^{2 =}$ 85%). On these measures, athletes with a HOC did not differ significantly from controls, Hedge's g = 0.15, z = 0.40, p = 0.69.

Verbal and Visual Memory — encoding

Clinical tests

Tests used to assess verbal memory (encoding) were found to be appropriately homogenous, $\tau^2 = 0.03$, df (3), $p = 0.24$; $I^2 = 29\%$. No group difference was found, Hedge's g = 0.11, z = 0.67, $p = 0.51$ (see Fig. 10).

Visual memory (encoding) was assessed by different versions of the Brief Visuospatial Memory Test (BVMT) across studies. Outcome measures were found to be appropriately homogenous, $\tau^2 = 0.00$, df (3), $p = 0.85$; $I^2 = 0\%$. Athletes with a HOC performed significantly worse relative to controls (Hedge's g = -0.44, z = 2.35, $p = 0.02$), with a small to medium size effect (Cohen, 1988). This is the only significant test in our meta-analysis (see Fig. 11).

Verbal and Visual Memory — storage

Screening tests

The ImpACT subtest used to assess verbal memory (storage) was found to be appropriately homogenous, $\tau^2 = 0.00$, df (3), $p = 0.99$; $I^2 = 0\%$. No group difference on these tests was observed, Hedge's g = 0.05, z = 0.44, $p = 0.66$ (see Fig. 12).

The ImpACT subtest used to assess visual memory (storage) was found to be appropriately homogenous, $\tau^2 = 0.00$, df (3), $p = 0.78$; $I^2 = 0\%$. No difference was found, Hedge's g = -0.17, z = 1.42, $p = 0.16$ (see Fig. 13), but once again we notice a tendency. Even if not significant, we that scores of athletes with a HOC seem to differ from the controls when assessed with visual measures rather than on verbal measures.

Verbal and Visual Memory — retrieval

Clinical tests

Tests used to assess verbal memory (retrieval) did not violate assumptions of homogeneity, $\tau^2 = 0.00$, df (3), $p = 0.38$; $I^2 = 2\%$. No significant group difference was observed, Hedge's g = -0.09, z = 0.49, $p = 0.63$ (see Fig. 14).

Tests used to assess visual memory (retrieval) were found to be appropriately homogenous ($\tau^2 = 0.01$, df (2), $p = 0.35$; $I^2 = 6\%$). No significant group difference was observed, Hedge's g = -0.09, z = 0.39, $p = 0.70$ (see Fig. 15).

Discussion

The aim of this meta-analysis was to determine the long-term cognitive impact of sports concussions in college-age male athletes. We generated 14 forest plots for which data were divided by the type of neuropsychological test (clinical, screening and experimental) and by cognitive domains (broad domains: processing speed, focal selective attention, executive functions and episodic memory). Our results show that there is no cognitive impact of sports concussions on a majority of the domains. Only one analysis was significant. The results of athletes with a HOC differed from those without a HOC on visual memory encoding. Further, we found that the literal conditions (simple and switch) of the Regensburger Verbal Fluency Test seem to discriminate athletes with a HOC and controls. The other cognitive domains were not significant.

Before addressing the summary effects from the forest plots, it is important to consider the assumption of heterogeneity. First, low heterogeneity was found for all but two measures. This supports the effectiveness of our classification strategy. Nevertheless, we observed significant heterogeneity for two subdomains of executive functions (EFs): set-shifting and interference management and response inhibition. This may be due to the fact that different studies report different outcome measures for the same tests. For example, Baune, Czira, Smith, Mitchell et Sinnamon (2012) analyzed ‘total errors’ and ‘non-perseverative errors’ scores from the same EFs test, and showed that only ‘total errors’ was significantly affected in their sample of adolescents with a major depressive disorder compared to controls. In fact, these different outcome measures could even reflect different cognitive processes.

Because heterogeneity was low, we can interpret our summary effects. Only one summary effect from the 14 analyses was significant. Immediate visual memory had a significantly small to medium effect. Our results suggest that athletes with a HOC could exhibit persistent difficulties with visual learning assessed by the Brief Visuospatial Memory Test (Original and Revised). This is in line with the results of Mangels, Craik, Levine, Schwartz et Stuss (2002) that indicate that participants with a mTBI who were three to four years post injury still made significantly more errors than controls on a visual memory task. Moreover, Master et al. (1999) found that 27% of athletes with a HOC had moderate to severe deficits on visual learning as assessed by the Complex Figure Test. On one hand, these results could be explained by a reduction in perceptual attention that may interfere with learning visual items (Moore & al., 2017). This is consistent with Ellemberg, Henry, Macciocchi, Guskiewicz et Broglio (2009) who conclude that athletes with a HOC present some impairments in visual attention. On the other hand, some authors suggest that verbal learning difficulties could be due to an alteration in executive functioning (planning, working memory) and result in subtle deficits in executive memory (Oldenburg, Lundin, Edman, Nygren de Boussard & Bartfai, 2016). In fact, they found group difference on a verbal memory test at the stage of encoding, not retrieval, just like us with visual material. Indeed, some studies provide evidence for persistent impaired executive functioning when tested with visual and spatial working memory tasks in both mTBI with post-concussive syndrome and athletes with a HOC (Sterr, Herron, Hayward, & Montaldi, 2006; Helmich & al., 2015; Ellemberg & al., 2007). Taken together, it is possible that the long-term impaired performance on a test of visual learning revealed by the present meta-analysis could be related to a failure in visual attention and in certain aspects of executive functioning. It is also possible that it represents a specific impairment in visual learning.

The impaired performance in visual encoding found in the present meta-analysis could be especially problematic for athletes, as they engage in sporting events that greatly solicit visual cognitive processes. For example, anticipating players' movements or even considering their own movements requires, among other things, a fine visual analysis, as well as visual working memory. From a clinical point of view, demonstrating long-term impaired performance at this level could therefore result in a significant functional handicap. Thus, clinicians need more sensitive measures to detect possible ongoing functional impairments (Karr, Areshenkoff & Garcia-Barrera, 2014).

The present meta-analysis showed any significant difference between athletes with a HOC and controls on the other cognitive domains (processing speed, focal selective attention, EFs—strategy generation and regulation—response inhibition, verbal memory—encoding and retrieval and visual memory—retrieval). This is not surprising given that the sports concussion literature rarely reports persistent impairments. Nevertheless, within each study, there is often at least one measure that significantly distinguishes the two groups. When the results of studies are considered individually, there is some evidence of persistent impaired performance in executive functions (Master 1999, Pontifex & al., 2009; Wall & al., 2006) and verbal memory (Kemp & al., 2016; Killam & al., 2005). Although, the meta-analyses for the executive functions domains were not significant, there is evidence from two studies that verbal fluency performance is impaired in athletes with a HOC. Specifically, we found that athletes with a HOC performed worse than controls on the literal conditions (simple and switch) of the Regensburger Verbal Fluency Test. Mangels et al. (2002) also report poorer scores on the literal condition of a verbal fluency test among mTBI participants several years after their injury. In the same line, McCrea et al. (2003) found a poorer performance on a verbal fluency test among athletes with a HOC relative to controls 90 days following a sports concussion. Taken together, these findings suggest that verbal fluency could likely be a clinically relevant tool for discriminating athletes with a HOC from those without a HOC. Moreover, the literal condition should be privileged compared to category conditions (Cralidis & Lundgren, 2014).

Even if the meta-analysis did not show significant differences for most cognitive domains, there is a tendency for athletes with a HOC to perform less well than controls in some domains. A tendency is defined as a result that is not significant but close to or equivalent to a small effect size. These domains include focal selective attention (clinical tests), strategy generation and regulation (clinical tests), set-shifting and interference management (clinical tests), and visual memory—storage (screening test). These tendencies suggest the possibility of other long-term cognitive impairments. There are several reasons that can explain why these domains were not significant. First, the currently available tests may not have the requisite level of difficulty to detect what it could be subtle impaired performances related to a HOC. For exemple, Baillargeon et al. (2012) found differences between athletes with a HOC and controls on electrophysiological measures but not on behavioral ones (neuropsychological tests). In fact, several studies provide evidence for neurophysiological alterations underlying certain cognitive processes in the absence of impaired performances on commercial clinical tests (Broglio, Pontifex, O'Connor & Hillman, 2009 ; Lavoie, Dupuis, Johnston, Leclerc & Lassonde, 2004 ; Ledwidge & Molfese, 2016; Thériault, De Beaumont, Tremblay, Lassonde & Jolicoeur, 2011). Therefore, researchers and clinicians should maximize their chance to detect cognitive impairments by adding more challenging conditions to their tests. For exemple, Sicard et al. (2018) added a more complex 2-back condition to the CogState test. This increased the load in working memory, making the already available 1-back task more complex. Their results show that differences between athletes with a HOC and controls only emerged during the 2-back condition and not the 1-back. Another reason why it seems to be important to increase task difficulty is that athletes could have a higher level of cognitive functioning. First, most studies assess collegiate athletes. Second, accumulating evidence suggests that the regular practice physical activity may have beneficial effects on cognitive functioning (Fernandes, Arida & Gomez-Pinilla, 2017). In summary, it is possible that the studies included in the present analysis did not use tests that had the requisite sensitivity to pick up subtle and persistent cognitive impairments stemming from sports concussion.

The clinical characteristics of the participants included in most studies can also be responsible for the lack of significant results. Many studies do not distinguish between athletes who fully recovered from sports concussion and those who may still present persisting symptoms or cognitive impairments. Most athletes recover from sports concussion within a week or two, whereas a minority will present persistent symptoms (McCrory & al., 2017).

Therefore, these athletes with persistent cognitive impairments could be hidden with the group comparisons.

Belanger et al. (2010) who performed a meta-analysis sharing a similar objective found significant small effect sizes for executive functions (assessed as a unique cognitive domain) and delay memory (assessed by combining both verbal and visual tests). A small effect size was also found for immediate memory, but it was not significant. Theses findings contrast with those from the present meta-analysis, where the only significant cognitive domain was the immediate visual memory. In the present meta-analysis, effect sizes for executive function and episodic memory (storage) were small but not significant. Although some methodological aspects differ between the Belanger et al. (2010) study and ours (e.g., executive function divided into subdomains, memory divided into verbal and visual subdomains, a control group without a HOC), the main conclusions are similar and indicate a persistent vulnerability in executive functions and episodic memory following sports concussions. This is in line with results from McIness, Friesen, MacKenzie, Westwood & Boe (2017) that found that a large proportion of individuals with a single mTBI demonstrated measurable impairments in various cognitive domains including executive function and learning/memory.

Limits

All studies included in the present meta-analysis included male college-aged athletes whilst a minority also included some female athletes (n= 6). We noticed that female athletes are quasi-absent from the studies. Considering that they practice sport as much as males, their exclusion from the studies is problematic. The little that is known about concussion in female athletes suggestions that they are more at risk than men to sustain this injury (Dick, 2009) and that they are more vulnerable to persistent cognitive symptoms (Sicard & al., 2018). As such, our results can only be extended to male athletes. They do not consider other populations like women, younger or older athletes and individuals who sustain non-sport concussion. Further, in our research the time since the last sports concussion was very heterogeneous (M = 22.56 months, SD = 22.29). This imposes a limit to the understanding of long-term cognitive functioning as several uncontrolled factors can play a role at different stages of the recovery (e.g., major depressive disorder due to a loss). Moreover, the cross-sectional nature of studies favors the introduction of these confounds. Even if Pontifex et al. (2009) showed a correlation between the number of previous concussions and long-term impaired performances, there is still a need for prospective longitudinal investigation demonstrating causation. Furthermore, most included studies relied upon self-report HOC. While this was necessary, it likely introduces biases due to errors in retrospective memory (Belanger & al., 2010). For example, some athletes may underestimate or perhaps over estimate symptoms they had at the time of injury or the number of sports concussion sustained.

This meta-analysis has also some methodological limitations. Although we tried to control for it, the publication bias remains unavoidable, even if we tried to control it by combining two search strategies. Another limit in our study may be the categorization of neuropsychological measures into specific cognitive domains. Any given test likely solicits several cognitive domains and different tests may be used to evaluate the same domain. Moreover, in our meta-analysis we choose to include studies where athletes with a HOC were compared to controls; however, athletes would be compared to the normative data in the clinical setting. Indeed, most of the neuropsychological tests used in sports concussion assessment and research use non-sports population’s norms (Ellemberg & al., 2009). In our meta-analysis, we only included studies with a control group that consisted of athletes without a HOC, which makes it possible to compare groups that share similar characteristics, including level of education, socio-economic status and physical condition, which all can influence cognitive function. Considering that, in our sample athletes with a HOC significantly performed poorer than controls on a visual learning task, but it does not necessarily mean that it represents a cognitive deficit as it is defined in clinical neuropsychology (an individual score that is below two standard deviations from the norm's mean). Finally, data for working memory were not sufficient to create an effect size for this domain. This would have been interesting since there is some evidence of working memory impairment following sports concussions (Helmich & al., 2015; Thornton & al., 2008).

Future Directions

The present study raises several methodological issues regarding the current literature, which should be considered for future research on long-term cognitive impact of sports concussion in athletes. First, even it is important to bear in mind that most individuals who sustain sports concussion seem to experience a relatively quick recovery from their injury, it is also important to recognize that some of them could endure long-term cognitive impairments. To be able to detect them and help them to manage their persistent symptoms in clinical settings, studies need to distinguish subgroups of athletes with a HOC. In the field of mild traumatic brain injuries, a difference between participants with and without persistent subjective symptoms is made and results show those with symptoms are more likely to have long-term cognitive impairments, whereas those without symptoms do not (Oldenburg & al., 2016; Dean & Sterr, 2013; Helmich & al., 2015). van der Horn et al. (2019) suggest others way to differentiate these subgroups, for example, using the heart rate variability biomarkers which could be interesting considering the fact that athletes could minimize their symptoms. It also appears to be necessary to investigate long-term cognitive functioning in female athletes. Moreover, further research should narrow TSI to allow for a better understanding of recovery. Besides, identifying or creating more complex cognitive tasks that challenge athletes would enable researchers and clinicians to capture potential subtle impairments. It is also possible to create a complex assessment environment. For exemple, McGrath et al. (2013) showed that athletes who did not present cognitive impairments when assessed at rest, presented impairments following an acute bout of moderate exercise.

Conclusion

The aim of this meta-analysis was to investigate long-term cognitive performances in college-aged athletes with one or more concussions compared to controls without a history of concussion. The results showed that most individuals who sustain sports concussions seem to experience a relatively quick recovery from their injury, which is consistent with the literature (Belanger & al., 2010; Broshek, De Marco & Freeman, 2015). However, it is important to bear in mind that a minority of athletes could experience long-term cognitive impairments. In our meta-analysis, this could have resulted in the significantly cognitive difference between athletes with and without a HOC in immediate visual memory, assessed by the BVMT(-R). The Regensburger Verbal Fluency Test also appeared to be a interesting clinical test, especially the literal condition. In clinical settings, to be able to detect athletes who suffer from long-term cognitive impairments and help them to manage their condition, it is therefore all the more important that future research's attempt to differentiate athletes who recovered from sports concussion from those who do not.

Finally, this work makes it possible to contribute at least to a better understanding of the cognitive consequences of sports concussions and give clinicians some clues to assess athletes with a HOC. But above all, it allows highlighting the methodological limitations of current studies and guide future research. Lastly, the combination of different research strategies may be helpful to conduct a thorough meta-analysis, at least in the field of sports concussion.

Compliance with ethical standard

The authors have no conflict of interests or funding to declare.

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Tables

Table 1: Classification of the neuropsychological measures into cognitive domains

Cognitive domains		*Tests (measures)*
PROCESSING SPEED		ImPACT (reaction time); RBANS (attention); SDMT (total correct)
ATTENTION	*Alert*	.
	Sustained attention	.
	Focalized attention	Oddball tasks (target response accuracy); PSU (total correct)
	Divided attention	.
EXECUTIVE FUNCTIONS	*Prospective Working Memory*	.
	Strategy Generation and Regulation	COWAT (total correct); Ruff figural fluency test (total correct); Verbal fluency test (total correct—categorizes + letters); Verbal fluency test (total correct—letters)
	Set-Shifting and Interference	Color Trail B (time); D-KEFS color word interference test

	Management	(switching condition—time); Oddball task (rare target reaction time); TMT B (time); Verbal fluency test (total correct—letters switching); Visual working memory task (reaction time—rare target—four items)
	Task Analysis	.
	Response Inhibition	ImPACT (impulse control)
	Self-Monitoring and Self-Maintenance	.
EPISODIC MEMORY	*Encoding*	AVLT (learning); BVMT (learning) ; BVMT-R (learning) ; HVLT (learning) ; RBANS (immediate memory)
	Storage	ImPACT (visual memory)
	Retrieval	AVLT (delay recall); BVMT (delay recall) ; BVMT-R (delay recall) ; RBANS (delay memory)

AVLT, Auditory verbal learning test; BVMT(-R), Brief visuospatial memory test (revised); COWAT, Controlled Oral Word Association Test; D-KEFS, Delis–Kaplan Executive Function System; HVLT, Hopkins Verbal Learning Test; ImPACT, Immediate *post-concussion assessment and cognitive test; PSU, Penn State Cancellation Test; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SDMT, Symbol Digit Modalities Test; TMT, Trail making test*

Table 2: Study characteristics

Studies	*HC (n)*	*HC male: number (%)*	*HC age in years: mean (SD)*	*HOC (n)*	*HOC male: number (%)*	*HOC age in years: mean (SD)*	*HOC number of concussions: mean (SD)*	*HOC TSI in months: mean (SD)*	*Type of diagnostic*
Bruce (1), 2009	560	100	19.31 (1,07)	60	100	19.59 (1,13)	3.58 (1,12)	Minimum six months	Self-reported
Bruce (2), 2009	292	100	19.32 (1,51)	27	100	19.88 (1,61)	3.81 (1,55)	Minimum six months	Self-reported
Baillargeon, 2012	15	100	23.40 (2,10)	15	100	23.30 (3,30)	1.5 (.80)	6.30 (3,50)	Diagnosed
Broglio, 2009	44	59,6	19.40 (1,30)	46	84,9	20.00 (1,20)	1.70 (1,10)	40.80 (36,00)	Self-report of diagnosed concussions
De	15	100	22.50	15	100	23.46	2.80 (1,32)	31.47	Self-

Beaumont, 2007			(2,53)			(2,67)		(22,03)	reported
Gardner, 2010	39	100	23.90 (3,54)	34	100	22.79 (2,65)	5.24 (2,44)	18.41 (22,06)	Self-reported
Gosselin, 2009	11	64	22.60 (2,40)	10	70	24.30 (6,10)	4.6 (1,72)	4.40 (3,16)	Self-reported and diagnosed for the last concussion
Lavoie, 2004	10	100	21.60 (0,88)	10	100	21.40 (1,00)	2.60 (0,68)	9.90 (6,70)	Self-reported
Leveille, 2017	15	100	21.44 (1.97)	10	100	21.59 (1.89)	2.80 (0.92)	24.14 (9.05)	Self-reported
List, 2015	21	90	25.70 (5,20)	20	90	25.50 (5,30)	2.90 (1,50)	24.53 (17,63)	Self-reported

Moore, 2017	19	100	23.16 (0.21)	14	100	23.36 (0.26)	1.86 (0.90)	27.30 (3.60)	Diagnosed
Parks, 2015	50	50	19.70 (1.60)	48	79	20.50 (2.20)	1.70 (1.10)	50.40 (40.80)	Self-report of diagnosed concussion
Singh, 2014	25	100	20.28 (1,43)	25	100	21.16 (1,31)	N/A	8.88 (14.41)	Diagnosed
Terry, 2012	20	100	20.40 (1.60)	20	100	20.30 (1.17)	3.15 (1.18)	19.60 (18.93)	Self-reported
Theriault, 2009	10	100	22.10 (1.40)	10	100	22.90 (3.30)	2.50 (0.70)	33.20 (15.40)	Self-reported and diagnosed
Theriault, 2011	21	100	21.67 (2.72)	16	100	21.56 (2.45)	1.37 (0.50)	26.94 (21.20)	Self-reported

Thoma, 2015	53	Majority of male	20.40 (1.29)	24	Majority of male	20.16 (1.44)	1.41 (0.58)	30.03 (24.89)	Self-reported
Wilke, 2017	22	91	26.10 (5,40)	17	88	24.20 (2,80)	3.10 (1,60)	21.20 (13,50)	Self-reported

HC, Healthy controls; HOC, Athletes with a history of concussion; n, Sample size; TSI, Time since injury

Table 3: Meta-analysis of cognitive domains

			Meta-analysis (Random model) Mean (95 % CI)				*Test of heterogeneity*		
					Clinical tests				
Cognitive domains	*Study N*	*Participant N*	*SMD*	*Lower*	*Upper*	*p*	I^2	T^2	*p*
Processing speed	10	575	-0.12	-0.35	0.12	0.34	17%	0.02	0.29
Selective attention	6	158	-0.23	-0.55	0.08	0.15	0%	0.00	0.98
EFs—Strategy Generation and Regulation	10	582	-0.20	-0.45	0.05	0.12	26%	0.04	0.20
EFs—Set-Shifting and Interference Management	10	582	-0.17	-0.49	0.15	0.29	52%	0.13	0.03*

Verbal memory—Encoding	4	439	0.11	-0.22	0.44	0.51	29%	0.03	0.24
Visual Memory — Encoding	4	117	-0.44	-0.81	-0.07	0.02*	0%	0.00	0.85
Verbal memory—Retrieval	4	125	-0.09	-0.45	0.27	0.63	2%	0.00	0.38
Visual Memory — Retrieval	3	80	-0.09	-0.55	0.37	0.70	6%	0.01	0.35
				Screening tests					
Cognitive domains	*Study N*	*Participant N*	*SMD*	*Lower*	*Upper*	*p*	I^2	T^2	*p*
Processing speed	5	910	0.10	-0.00	0.29	0.30	9%	0.00	0.36
EFs—Response inhibition	3	200	0.15	-0.60	0.91	0.69	85%	0.38	0.0001*
Verbal memory—Encoding	4	290	0.05	-0.18	0.29	0.66	0%	0.00	0.99

Visual Memory — Encoding	4	290	-0.17	-0.41	0.06	0.16	0%	0.00	0.87
					Experimental tasks				
Cognitive domains	*Study N*	*Participant N*	*SMD*	*Lower*	*Upper*	*p*	I^2	T^2	*p*
Selective attention	5	271	-0.07	-0.35	0.21	0.61	21%	0.02	0.28
EFs—Set-Shifting and Interference Management	2	57	0.50	-0.03	1.03	0.07	0%	0.00	0.88

SDM, Standardized mean difference; EFs, Executive functions

Figures

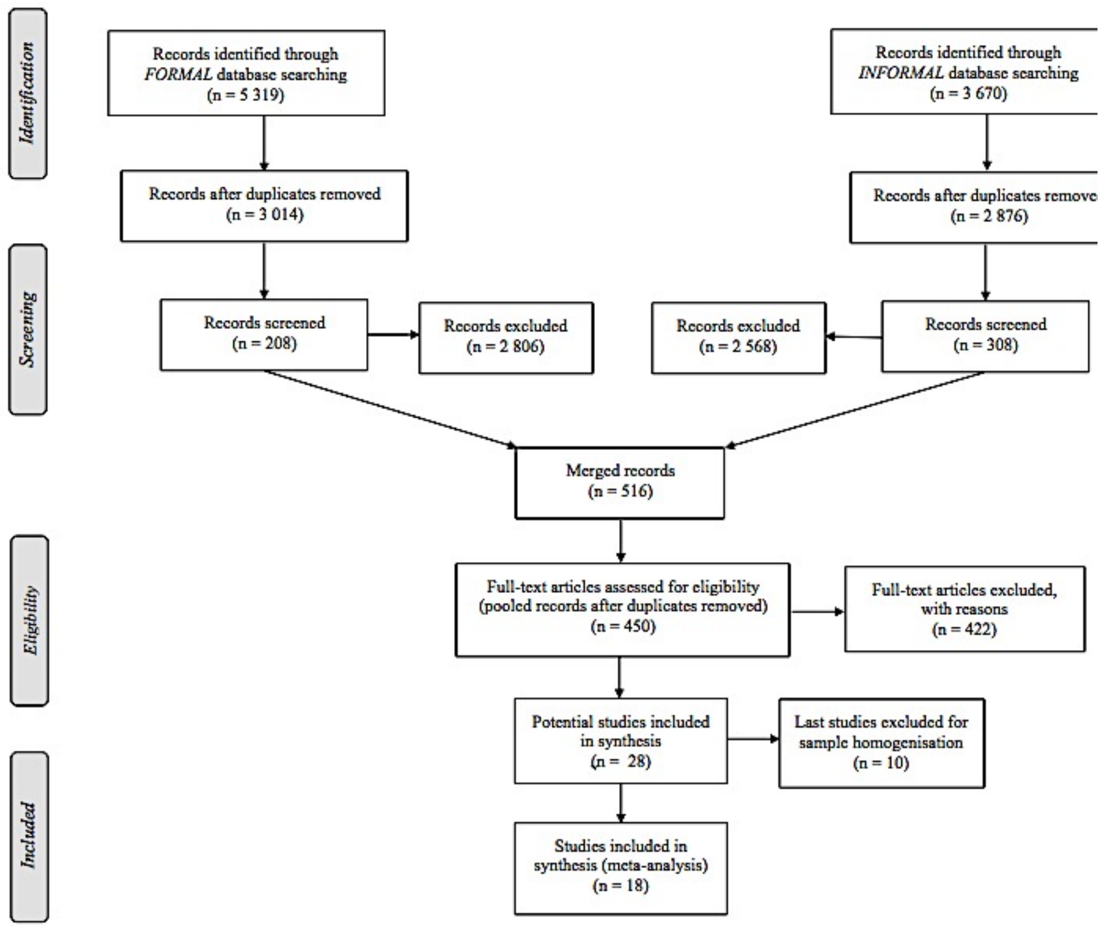

Figure 1: Flowchart of study selection

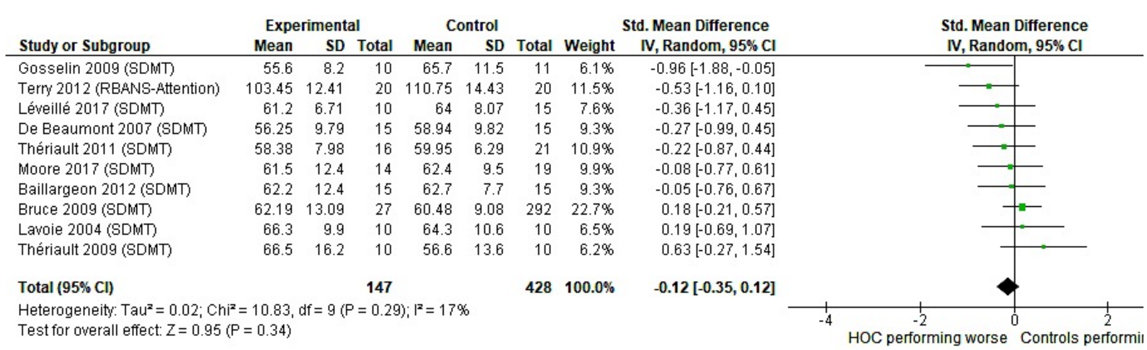

Figure 2: Forest plot for processing speed assessed by clinical tests

CI, Confidence interval; HOC, Athletes with a history of concussion; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SD, Standard deviation; SDMT, Symbol Digit Modalities Test

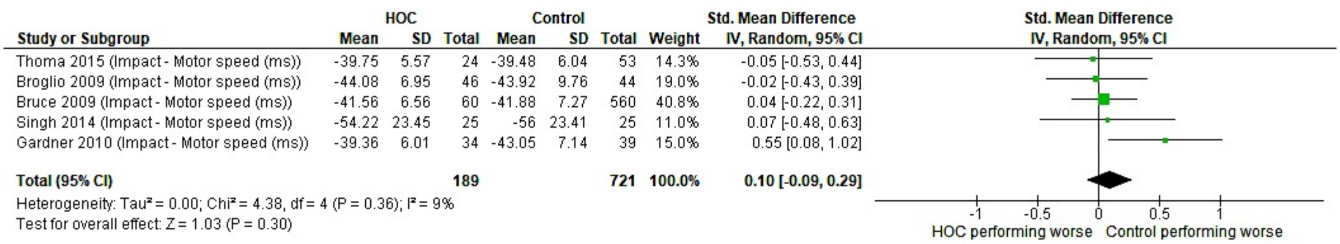

Figure 3: Forest plot for processing speed assessed by screening tests

CI, Confidence interval; HOC, Athletes with a history of concussion; ms, Milliseconds; SD, Standard deviation

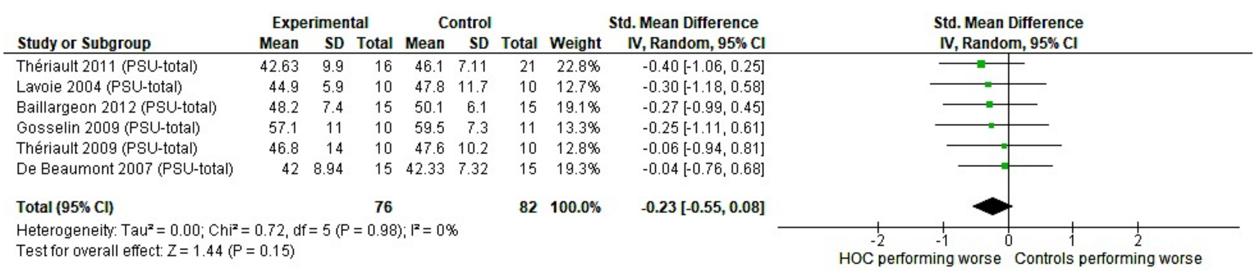

Figure 4: Forest plot for focal selective attention assessed by clinical tests

CI, Confidence interval; HOC, Athletes with a history of concussion; SD, Standard deviation; PSU, Penn State Cancellation Test

Study or Subgroup	HOC Mean	HOC SD	HOC Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Broglio 2009 (Novelty Oddball - Target accuracy)	95	6.2	46	97.2	5.2	44	30.8%	-0.38 [-0.80, 0.04]
Moore 2017 (Oddball - Target Accuracy)	96.4	3.9	14	97.1	2.5	19	14.0%	-0.22 [-0.91, 0.48]
De Beaumont 2007(Oddball-Frequent Target Accuracy)	97.5	2.9	15	97.9	1.6	15	13.2%	-0.17 [-0.88, 0.55]
Thériault 2009 (Oddball - Target Accuracy)	96.6	3	10	95.4	8.5	10	9.2%	0.18 [-0.70, 1.06]
Parks 2015 (Oddball - Target Accuracy)	98.2	2.5	48	97.5	3.2	50	32.8%	0.24 [-0.16, 0.64]
Total (95% CI)			**133**			**138**	**100.0%**	**-0.07 [-0.35, 0.21]**

Heterogeneity: Tau² = 0.02; Chi² = 5.03, df = 4 (P = 0.28); I² = 21%
Test for overall effect: Z = 0.51 (P = 0.61)

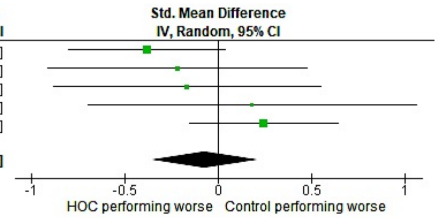

Figure 5: Forest plot for focal selective attention assessed by experimental

CI, Confidence interval; HOC, Athletes with a history of concussion; SD, Standard deviation

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Wilke 2017 (Verbal Fluency - Letters)	8	3	17	12	5	22	10.5%	-0.92 [-1.59, -0.25]
List 2015 (Verbal fluency - Letters)	9	4	20	12	5	21	11.4%	-0.65 [-1.28, -0.02]
Léveillé 2017 (Verbal Fluency (Total))	29.13	5.36	10	32.44	6.47	15	7.7%	-0.53 [-1.34, 0.29]
Gosselin 2009 (Graphic fluency (Total))	65	11.6	10	69.4	9.2	11	7.0%	-0.41 [-1.27, 0.46]
Baillargeon 2012 (COWAT)	39.1	10.5	15	41.7	12.1	15	9.4%	-0.22 [-0.94, 0.49]
Bruce 2009 (COWAT)	42.63	10.43	27	42.22	10.69	292	20.1%	0.04 [-0.36, 0.43]
Thériault 2009 (Verbal Fluency (Total))	33.8	5.9	10	33.4	9	10	6.8%	0.05 [-0.83, 0.93]
De Beaumont 2007 (Verbal Fluency (lett+categ))	35.75	9	15	34.72	10.06	15	9.4%	0.10 [-0.61, 0.82]
Lavoie 2004 (COWAT)	43.2	11.5	10	41.2	11.2	10	6.8%	0.17 [-0.71, 1.05]
Thériault 2011 (Verbal Fluency (Total))	37.13	6.24	16	34.9	10.01	21	10.8%	0.25 [-0.40, 0.91]
Total (95% CI)			**150**			**432**	**100.0%**	**-0.20 [-0.45, 0.05]**

Heterogeneity: Tau² = 0.04; Chi² = 12.17, df = 9 (P = 0.20); I² = 26%
Test for overall effect: Z = 1.56 (P = 0.12)

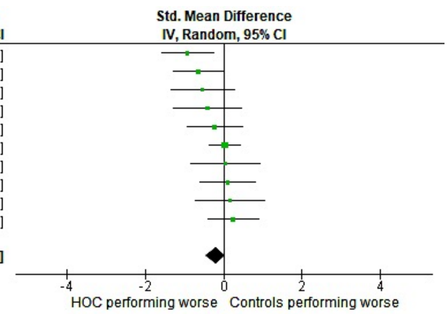

Figure 6: Forest plot for EFs — strategy generation and regulation assessed by clinical tests

CI, Confidence interval; COWAT, Controlled Oral Word Association Test; HOC, Athletes with a history of concussion; SD, Standard deviation

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
List 2015 (Verbal Fluency - Letters switching)	8	3	20	11	4	21	11.1%	-0.83 [-1.47, -0.19]
Wilke 2017 (Verbal Fluency - Letters switching)	8	3	17	11	4	22	10.8%	-0.82 [-1.48, -0.15]
Léveillé 2017 (Stroop D-KEFS alternance (time))	-51.9	6.08	10	-47.31	6.55	15	8.5%	-0.70 [-1.52, 0.13]
Gosselin 2009 (TMT-B)	-74.4	31.6	10	-65.9	40.3	11	8.2%	-0.22 [-1.08, 0.64]
Thériault 2011 (Color-Trail B)	-61.94	12.73	16	-59.52	16.74	21	10.9%	-0.16 [-0.81, 0.50]
Baillargeon 2012 (Color-Trail B)	-52.1	13.4	15	-50.6	11.6	15	10.0%	-0.12 [-0.83, 0.60]
Bruce 2009 (TMT-B)	-51.85	16.64	27	-52.1	15.85	292	15.5%	0.02 [-0.38, 0.41]
Lavoie 2004 (Color-Trail B)	-80	11	10	-82	13	10	7.9%	0.16 [-0.72, 1.04]
De Beaumont 2007 (Color-Trail B)	-62.62	7.58	15	-66.44	22.16	15	10.0%	0.22 [-0.49, 0.94]
Thériault 2009 (Color-Trail B)	-54	12.5	10	-66.7	9.5	10	7.2%	1.10 [0.14, 2.05]
Total (95% CI)			**150**			**432**	**100.0%**	**-0.17 [-0.49, 0.15]**

Heterogeneity: Tau² = 0.13; Chi² = 18.62, df = 9 (P = 0.03); I² = 52%
Test for overall effect: Z = 1.05 (P = 0.29)

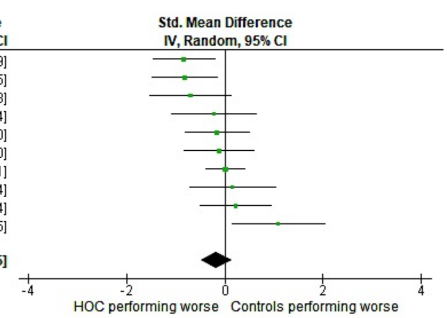

Figure 7: Forest plot for EFs — set-shifting and interference management assessed by clinical tests

CI, Confidence interval; D-KEFS, Delis–Kaplan Executive Function System;

HOC, Athletes with a history of concussion; SD, Standard deviation; TMT; Trail Making Test

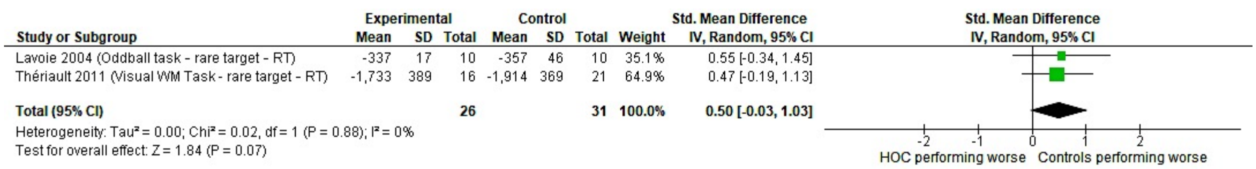

Figure 8: Forest plot for EFs — set-shifting and interference management assessed by experimental tasks

CI, Confidence interval; HOC, Athletes with a history of concussion; SD, Standard deviation; RT, Reaction time; WM, Working memory

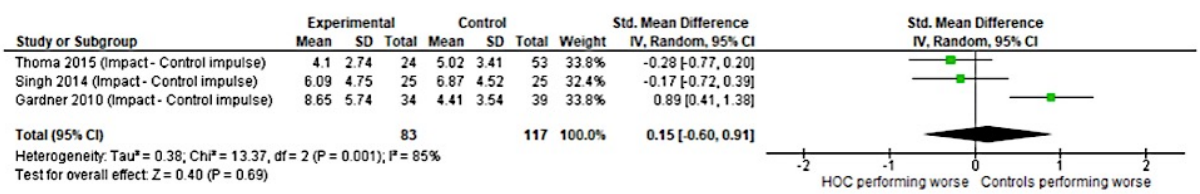

Figure 9: Forest plot for EFs — response inhibition assessed by screening tests

CI, Confidence interval; HOC, Athletes with a history of concussion; ImPACT, Immediate post-concussion assessment and Cognitive testing; SD, Standard deviation

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bruce 2009 (HVLT-Learning)	28	3.14	27	26.6	3.9	292	38.0%	0.36 [-0.03, 0.76]
List 2015 (AVLT-Learning)	55	6	20	58	9	21	21.0%	-0.38 [-1.00, 0.24]
Terry 2012 (RBANS-Immediate memory)	104.45	14.59	20	104.1	16.09	20	20.9%	0.02 [-0.60, 0.64]
Wilke 2017 (AVLT-Learning)	58	7	17	56	9	22	20.1%	0.24 [-0.40, 0.87]
Total (95% CI)			**84**			**355**	**100.0%**	**0.11 [-0.22, 0.44]**

Heterogeneity: Tau² = 0.03; Chi² = 4.20, df = 3 (P = 0.24); I² = 29%
Test for overall effect: Z = 0.67 (P = 0.51)

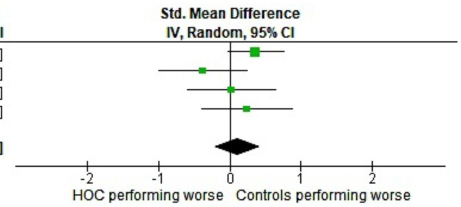

Figure 10: Forest plot for verbal memory—encoding assessed by clinical tests

AVLT, Auditory-Verbal Learning Test; CI, Confidence interval; HOC, Athletes with a history of concussion; HVLT; Hopkins verbal learning test; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SD, Standard deviation

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Baillargeon 2012 (BVMT-R- Learning)	30.9	4.7	15	32.1	2.9	15	26.3%	-0.30 [-1.02, 0.42]
De Beaumont 2007 (BVMT- Learning)	28.25	5.78	15	29.72	4.16	15	26.3%	-0.28 [-1.00, 0.44]
Thériault 2009 (BVMT-Learning)	29.3	2.7	10	31.6	3.3	10	16.4%	-0.73 [-1.64, 0.18]
Thériault 2011 (BVMT-learning)	28.38	4.48	16	30.86	4.4	21	31.0%	-0.55 [-1.21, 0.12]
Total (95% CI)			**56**			**61**	**100.0%**	**-0.44 [-0.81, -0.07]**

Heterogeneity: Tau² = 0.00; Chi² = 0.82, df = 3 (P = 0.85); I² = 0%
Test for overall effect: Z = 2.35 (P = 0.02)

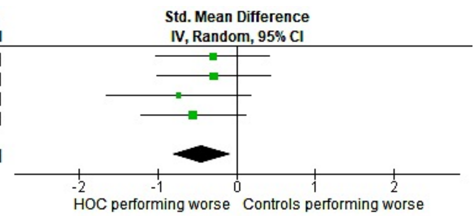

Figure 11: Forest plot for visual memory—encoding assessed by clinical tests

BVMT (R), Brief Visuospatial Memory Test (Revised); CI, Confidence interval; HOC, Athletes with a history of concussion; SD, Standard deviation

Study or Subgroup	HOC Mean	HOC SD	HOC Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Gardner 2010 (Impact - verbal memory)	0.85	0.12	34	0.85	0.09	39	26.1%	0.00 [-0.46, 0.46]
Thoma 2015 (Impact - verbal memory)	87.65	7.66	24	87.26	9.33	53	23.7%	0.04 [-0.44, 0.53]
Broglio 2009 (Impact - verbal memory)	90.36	8.67	46	89.56	10.29	44	32.3%	0.08 [-0.33, 0.50]
Singh 2014 (Impact - verbal memory)	59.65	28.65	25	57.04	29.07	25	17.9%	0.09 [-0.47, 0.64]
Total (95% CI)			**129**			**161**	**100.0%**	**0.05 [-0.18, 0.29]**

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 3 (P = 0.99); I² = 0%
Test for overall effect: Z = 0.44 (P = 0.66)

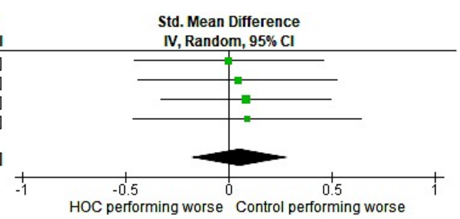

Figure 12: Forest plot for verbal memory—storage assessed by screening tests

CI, Confidence interval; HOC, Athletes with a history of concussion; ImPACT, Immediate post-concussion assessment and Cognitive testing; SD, Standard deviation

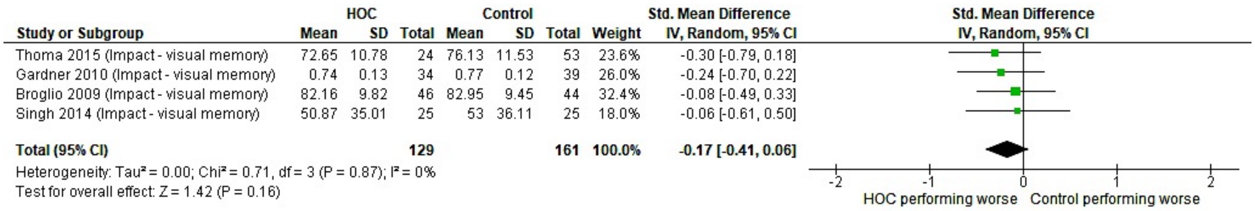

Figure 13: Forest plot for visual memory—storage assessed by screening tests

CI, Confidence interval; HOC, Athletes with a history of concussion; ImPACT, Immediate post-concussion assessment and Cognitive testing; SD, Standard deviation

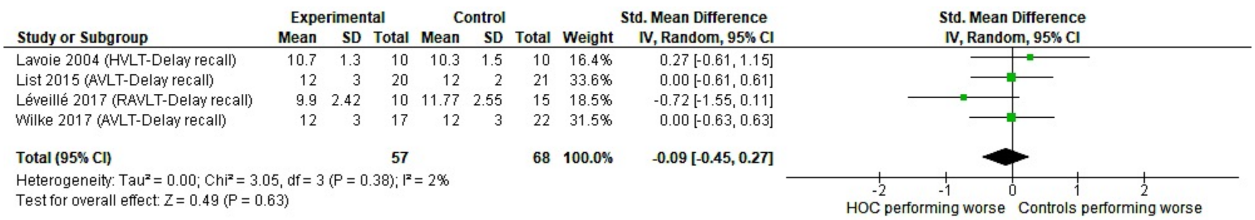

Figure 14: Forest plot for verbal memory—retrieval assessed by clinical tests

AVLT, Auditory-Verbal Learning Test; CI, Confidence interval; HOC, Athletes with a history of concussion; HVLT; Hopkins verbal learning test; RAVLT, Rey auditory verbal learning test; SD, Standard deviation

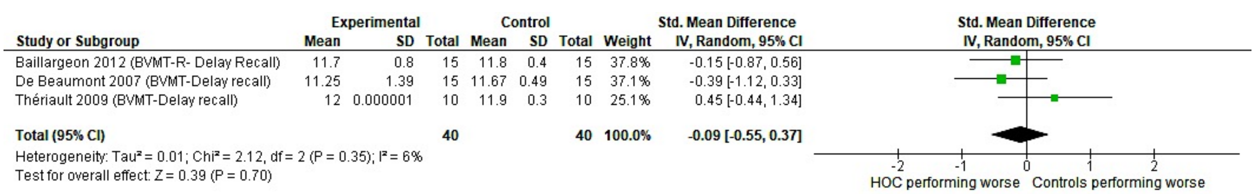

Figure 15: Forest plot for visual memory—retrieval assessed by clinical tests

BVMT (R), Brief Visuospatial Memory Test (Revised); CI, Confidence interval; HOC, Athletes with a history of concussion; SD, Standard deviation

Appendix A

The PRISMA check list 2009

Section/topic	#	Check list item	Yes or No
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Yes
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.	Yes
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Yes
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Yes
METHODS			
Protocol and	5	Indicate if a review protocol exists, if and where it can be accessed	No

registration		(e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of the follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Yes
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.	Yes
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Yes
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).	Yes
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.	Yes
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Yes
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.	Yes

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Yes
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	Yes
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).	No
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.	Yes
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.	Yes
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).	Yes
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.	Yes

Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Yes
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Yes
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).	Yes
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).	Yes
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Yes
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.	Yes

Appendix B

Details of the informal search conducted by GC: databases, dates and key words

1. PUBMED

- May 13, 2017
  - " concussion " OR " mTBI " AND " athlete " AND " cognitive testing " (N = 212)
  - " concussion " OR " mTBI " AND " athlete " AND " neuropsychological assessment " (N = 444)
- May 14, 2017
  - "concussion" OR "mTBI" AND "athlete" AND "cognitive testing" AND "college" (N = 59)
  - " concussion " OR " mTBI " AND " athlete " AND " long-term deficits " (N = 30)
  - " concussion " OR " mTBI " AND " athlete " AND " cognitive deficits " (N = 18)
  - " concussion " OR " mTBI " AND " athlete " AND " cognitive deficits " (N = 39)
  - " concussion " OR " mTBI " AND " athlete " AND " cognitive testing " (N = 68)
  - " concussion " OR " mTBI " AND " athlete " AND " chronic deficits " (N = 14)
- May 15, 2017
  - " concussion " OR " mTBI " AND " athlete " AND " cognition " (N = 277)

– “concussion” OR “mTBI” AND “athlete” AND “PCS” (N = 32)

- May 16, 2017

– “ concussion ” OR “ mTBI ” AND “ athlete ” AND “ outcome ” (N = 239)

- May 17, 2017

– “concussion” OR “mTBI” OR “mild traumatic brain injury” AND “university OR “college” AND “post-concussion syndrome” OR “PCS” OR “chronic” OR “long-term” AND “deficit” OR “cognitive” OR “cognition” OR “neuropsychological” (N = 967)

– “concussion” OR “mTBI” OR “mild traumatic brain injury” AND “university” OR college” AND “ Stroop task ” (N = 26)

– “concussion” OR “mTBI” OR “mild traumatic brain injury” AND “university” OR “college” OR “adult” AND “cognition” OR “deficit” OR “NP test” OR “neuropsychological assessment” AND “chronic” OR “long-term” OR “pervasive” (N = 572)

Total number of studies before duplication remove: N = 2997

Total number of studies after duplication removes: N = 1528

2. EMBASE

- May 18, 2017

– “exp concussion” OR “exp brain injury” (N = 151,493)

– “exp athlete” (N = 40,709)

– “exp psychologic test” OR “exp cognitive defect” OR “exp neuropsychological test” (N = 260,205)

– "exp concussion" OR "exp brain injury" AND "exp athlete" AND "exp psychologic test" OR "exp cognitive defect" OR "exp neuropsychological test" (N = 487)

Total number of studies after merging PUBMED and EMBASE and duplication remove: N = 2007

3. GOOGLE SCHOLAR

- May 20, 2017

– "Concussion athlete deficit" (N = 69)

- May 21, 2017

– "concussion athlete chronic college" OR "university" OR "amateur" OR "professional neuropsychological assessment" (N = 2,120)

4. WEB OF SCIENCE

- May 22, 2017

– "concussion" OR "brain injury" (N = 127,284)

– "cognit*" OR "neuropsychol*" OR "cognit*" OR "deficit" (N = 542,856)

– "athlete" OR "sport" (N = 132,644)

– "college" OR "university" OR "amateur" OR "professional" (N = 947,748)

– "concussion" OR "brain injury" AND "cognit*" OR "neuropsychol*" OR "cognit*" OR "deficit" AND "athlete" OR "sport" AND "college" OR "university" OR "amateur" OR "professional" (N = 458)

5. SCOPUS

- May 22, 2017

– TITLE-ABS-KEY “concussion” OR "brain” AND “ injury" AND ALL “athlete” OR “sport” AND ALL “neuropsych!” OR “cognit!” (N = 156)

6. Final duplication removes

Total number of studies before duplication remove: N = 3,670

Total number of studies after duplication removes: N = 2,876

Appendix C

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Appendix D

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Discussion

L'objectif de cette méta-analyse était de déterminer si un affaiblissement à long terme des capacités cognitives était présent lorsque des athlètes avec un historique d'une ou plusieurs commotions étaient évalués à l'aide de tâches neuropsychologiques. Les résultats montrent qu'à l'exception de l'apprentissage d'items visuels, les performances des athlètes avec un historique de CC ne diffèrent pas de celles des témoins, ce qui est en faveur de l'hypothèse qu'une majorité d'entre eux récupère relativement rapidement après une CC (Belanger & al., 2010 ; Broshek, De Marco & Freeman, 2015, McCrory & al., 2017).

Cette hypothèse est ainsi fondée sur des données statistiques, ce qui procure de la puissance aux résultats, mais n'exclue pas pour autant qu'une minorité d'individus risque de ressentir des symptômes persistants. En effet, il est possible qu'un sous-échantillon d'athlètes soit perdu dans les comparaisons de groupes. Iverson (2010) a d'ailleurs montré que les analyses statistiques peuvent masquer les différences individuelles. Or, ce sont ceux qui ne présentent pas une trajectoire de rétablissement dite « normale » qui consultent des professionnels de la santé tel que le neuropsychologue. Ce dernier, qui travaille à l'échelle de l'individu, cherche justement à appréhender cette différence inter (et intra) individuelle. Alors comment un neuropsychologue peut-il se servir des résultats de cette méta-analyse pour le guider dans sa pratique clinique ?

Bien que cette étude révèle un effet significatif au *Brief Visuospatial Memory Test* (BVMT), il n'est pas recommandé aux cliniciens d'utiliser ce test de manière isolée et de fonder leurs impressions cliniques sur un seul résultat. Le travail du neuropsychologue consiste justement à construire une évaluation complète où les différentes fonctions cognitives sont évaluées et où chaque fonction est testée à l'aide de plusieurs outils. Il s'agit également d'obtenir une vision plus globale d'un individu dans son contexte de vie singulier et d'utiliser son jugement clinique pour interpréter un ensemble de données. Ainsi, les résultats de cette méta-analyse orienteront davantage le neuropsychologue dans son choix des outils à utiliser auprès des athlètes avec un historique de CC. Il pourrait par exemple favoriser le BVMT-R par rapport à un autre test pour évaluer la mémoire épisodique visuelle. Il pourrait aussi être attentif à un éventuel écart entre les performances aux tâches visuelles vs. verbales. Il pourrait également accorder un intérêt tout particulier aux fluences verbales littérales par rapport aux fluences catégorielles, et éventuellement décider de faire une évaluation au-delà des méthodes standardisées sur cette condition.

Par ailleurs, pour le neuropsychologue qui s'intéresse à cette population, il s'avère pertinent de mieux comprendre le développement de ce que l'on appelle le syndrome post-commotionnel (SPC), terme qui peut être utilisé pour désigner ceux qui souffrent de symptômes persistants suite à une CC ou un TCC léger. Autant les étiologies physiologiques que psychologiques ont été considérées comme pouvant être la cause des symptômes persistants, ce qui a participé à l'émergence de la controverse sur le sujet au sein de la littérature scientifique (Ryan & Warden, 2003). Désormais, il est plutôt admis que le développement et le maintien de symptômes à long terme résulterait d'une interaction entre des facteurs physiologiques et psychologiques (Broshek, De Marco & Freeman, 2015).

Par exemple, Bramley et al. (2016) proposent une vision intégrée du syndrome post-commotionnel (SPC) comme résultant d'influences mutuelles entre les différents groupes de symptômes : symptômes liés à l'humeur, au sommeil, symptômes somatiques et cognitifs. Il recommande d'ailleurs une évaluation neuropsychologique complète, dans laquelle chaque élément qui pourrait intensifier les symptômes serait aussi considéré (e.g., histoire prémorbide). Ll Wood (2004) propose une manière plus dynamique de conceptualiser le SPC en élaborant un modèle de diathesis-stress (Figure 17) : plus la vulnérabilité biologique de base est grande, l'accident violent et les stresseurs environnementaux présents, plus l'athlète aura de chance de présenter des symptômes à long terme.

Plus récemment, van der Horn et al. (2019) exposent en détail différents facteurs physiologiques et psychologiques et explorent les interactions théoriques entre ces facteurs qui peuvent intervenir dans le développement et le maintien des symptômes à long terme. Ils expliquent par exemple que les blessures au niveau cellulaire engendrent une réponse inflammatoire, l'inflammation étant également liée à un niveau élevé de cortisol qui est associé au stress. La réaction au stress dépend elle-même en partie de facteurs psychologiques prémorbides, telle que la capacité à s'adapter à des évènements de vie difficiles. Or, les effets en aiguë du TCC léger ébranlent certains réseaux neuronaux impliqués dans la régulation émotionnelle, telle que le cortex préfrontal, ainsi le choc du traumatisme pourrait en soi impacter la réponse adaptative au stress (Figure 18). Ils résument ainsi : « *The interaction between cellular injury, inflammation and stress, mediated by pre-existent coping style or personality, might well be a key mechanism in the persistence of post-traumatic symptoms.* »[1] (van der Horn & al., 2019, p. 5). Notons qu'ici les modèles proposant une explication au SPC se basent sur le TCC léger toutes étiologies confondues. À notre connaissance, il n'existe pas

[1] Traduction libre : L'interaction entre la blessure cellulaire, l'inflammation et le stress, le tout émergeant chez un individu avec sa propre personnalité et ses propres stratégies d'adaptation, pourrait être un mécanisme clé pour expliquer la persistance des symptômes post-traumatiques.

de telles propositions uniquement centrées sur les CC, ce qui serait pourtant pertinent étant donné la spécificité de cette population.

Ainsi, pour comprendre cliniquement le développement de symptômes persistants chez un athlète, il faudrait prendre en compte : les mécanismes pathophysiologiques découlant directement de la CC ; l'influence des émotions sur le fonctionnement cognitif ; les facteurs psychologiques prémorbides (relations familiales, personnalité, stratégies d'adaptation, facteurs de stress psychosociaux...) ; les facteurs psychologiques actuels (stratégies d'adaptation, attentes, douleur, motivation, support et soutien social...) et les effets iatrogènes de la prise en charge (bénéfices secondaires, façon dont les différents professionnels reçoivent la plainte...).

De plus, la littérature actuelle nous informe sur les facteurs de risque de développement des symptômes à long terme. L'INESS (2018) recense différents facteurs à considérer dans le cadre d'un TCC léger : enjeux d'indemnisation ; personne de plus de 40 ans ; antécédents neurologiques ; antécédents de TCC léger ; antécédents de troubles du sommeil ; stresseurs prémorbides ; symptômes vestibulo-occulaires. Quant aux CC, le consensus de Berlin (McCrory & al., 2017) mentionne que la sévérité des symptômes initiaux, la présence de migraines et de symptômes dépressifs en phase aiguë, ainsi que des antécédents de migraines et de problèmes de santé mentale, sont des facteurs de risque de présenter des symptômes à long terme (au-delà d'un mois selon leur critères).

Enfin, il est intéressant d'évoquer le concept de réserve cognitive. Celui-ci a été proposé pour tenir compte de la discordance entre le degré de lésion cérébrale et ses manifestations cliniques. Autrement dit, pour un même degré de lésion, deux personnes ne vont pas présenter le même tableau clinique. Ainsi, le concept de réserve cognitive postule que certaines personnes sont plus résilientes que d'autres face à une lésion cérébrale, et ce, en raison de différences interindividuelles dans les processus cognitifs ou dans les réseaux neuronaux sous-jacents à l'exécution de tâches (Stern, 2009). Les indicateurs usuels de cette réserve cognitive sont les indices de quotient intellectuel, ainsi que les variables sociodémographiques, telle que le niveau d'éducation ou l'emploi occupé. Or, une étude récente montre une association entre un faible niveau de réserve cognitive (mesuré par le quotient intellectuel prémorbide, le niveau d'éducation et l'emploi occupé) et la présence de symptômes subjectifs persistants (< 3 mois) suite à un TCC léger (Oldenburg & al., 2016). Les auteurs suggèrent ainsi qu'un faible niveau de réserve cognitive pourrait être lié à un affaiblissement de la capacité à mobiliser des stratégies compensatoires, ce qui pourrait perturber la réalisation des tâches de la vie quotidienne et ainsi engendrer du stress.

Finalement, il est important de reconnaitre les enjeux cliniques associés au SPC. Ll Wood & al. (2004, p. 1136) l'expriment ainsi *« those with persisting symptoms may represent a notional minority, but the complex nature of their symptoms is clinically challenging, often intractable and usually requires attention from a range of health care professionals over many years »*[2]. Pour conclure, le SPC est un phénomène biopsychosocial complexe, pouvant significativement altérer la qualité de vie de cette « minorité misérable » (Ruff & al., 1994 cités par Rohling, Larrabee & Millis, 2012) et qui mérite, de ce fait, une attention toute particulière autant en clinique qu'en recherche. Ainsi les résultats de cette méta-analyse permettent de nourrir une réflexion qui va au-delà de l'objectif initial de cette recherche,

[2] Traduction libre : Ceux qui ont des symptômes persistants peuvent représenter une minorité nationale, mais la nature complexe de leurs symptômes représente un défi sur le plan clinique et nécessite habituellement l'attention d'une équipe multidisciplinaire durant des années

notamment en abordant ce travail sous un angle clinique qui pourrait s'avérer pertinent pour des neuropsychologues travaillant auprès d'athlètes avec un historique de CC.

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Figures

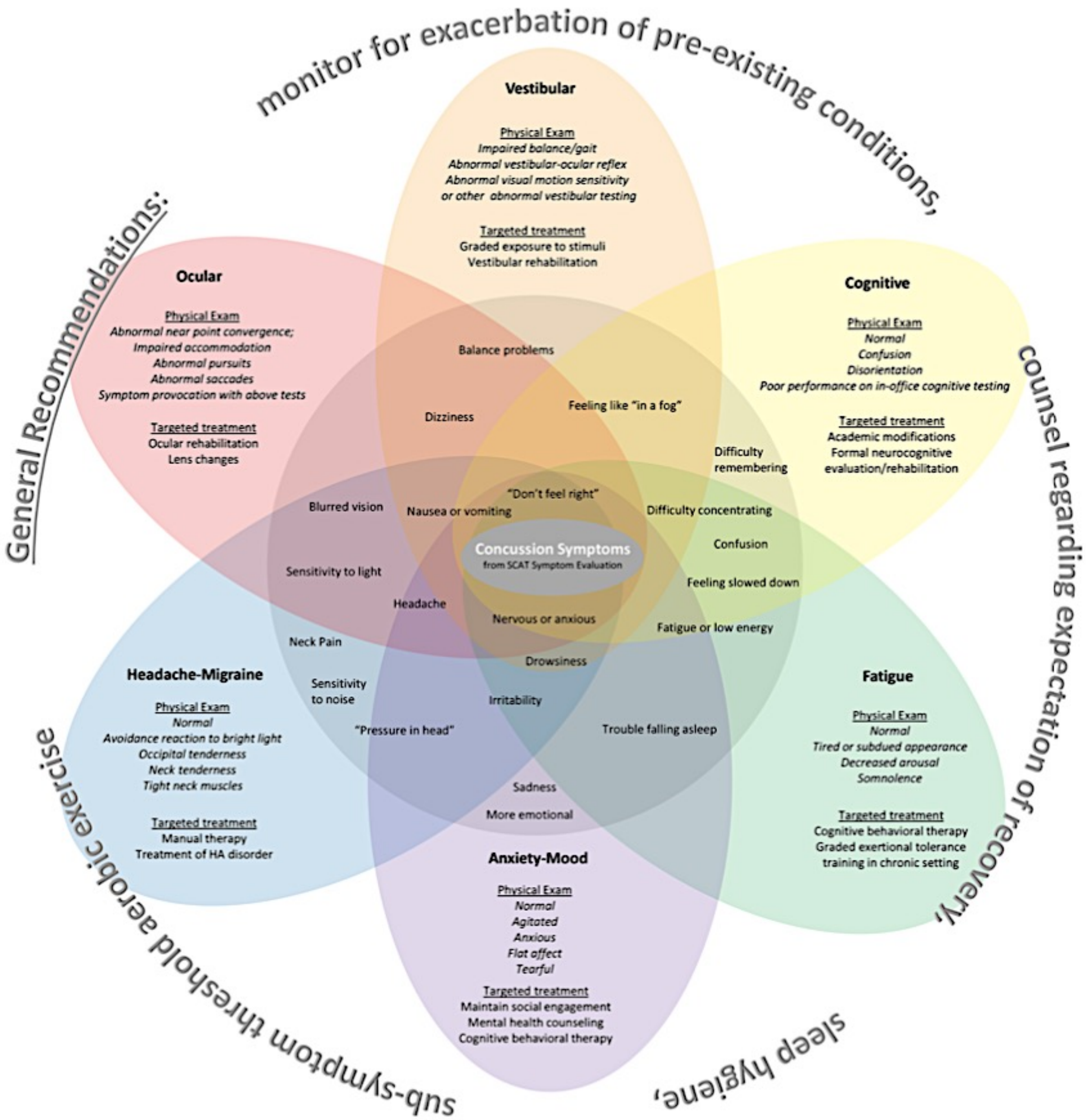

Figure 16 : Chevauchement des différents profils cliniques en fonction des symptômes éprouvés suite à un TCC léger ou une CC. *Note.* Tiré de « American Medical Society for Sports Medicine position statement on concussion in sport », by Harmon & al., 2019, *British Journal of Sports Medicine*, 53(4), 213-225.

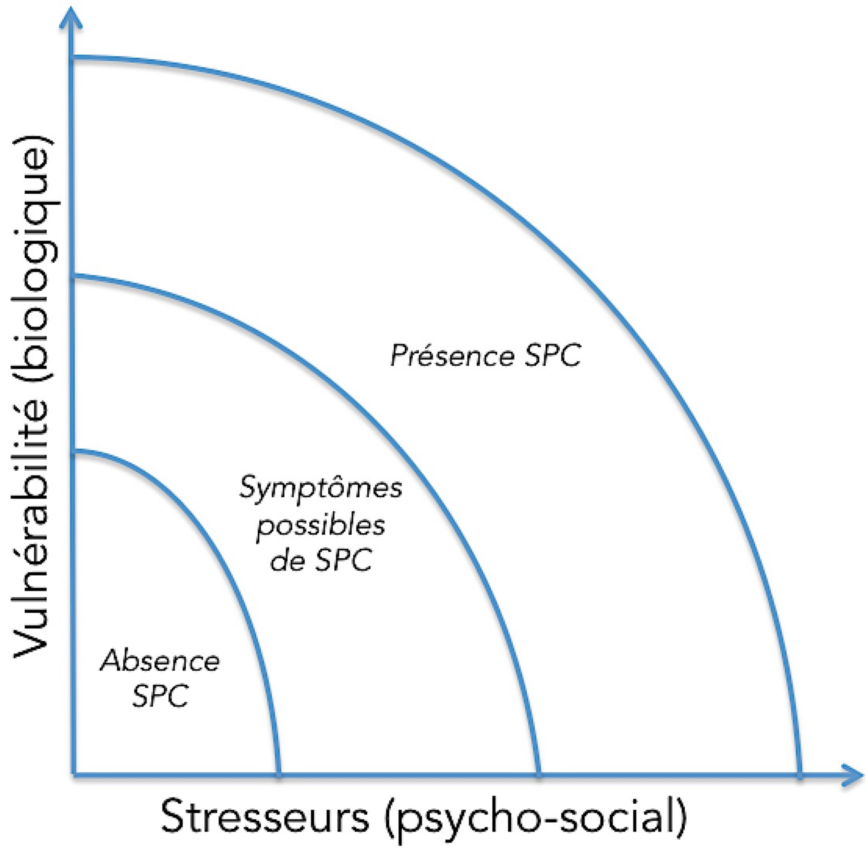

Figure 17 : Représentation du modèle de diathesis-stress proposé par LI Wood (2004)

SPC; Syndrome post-commotionnel

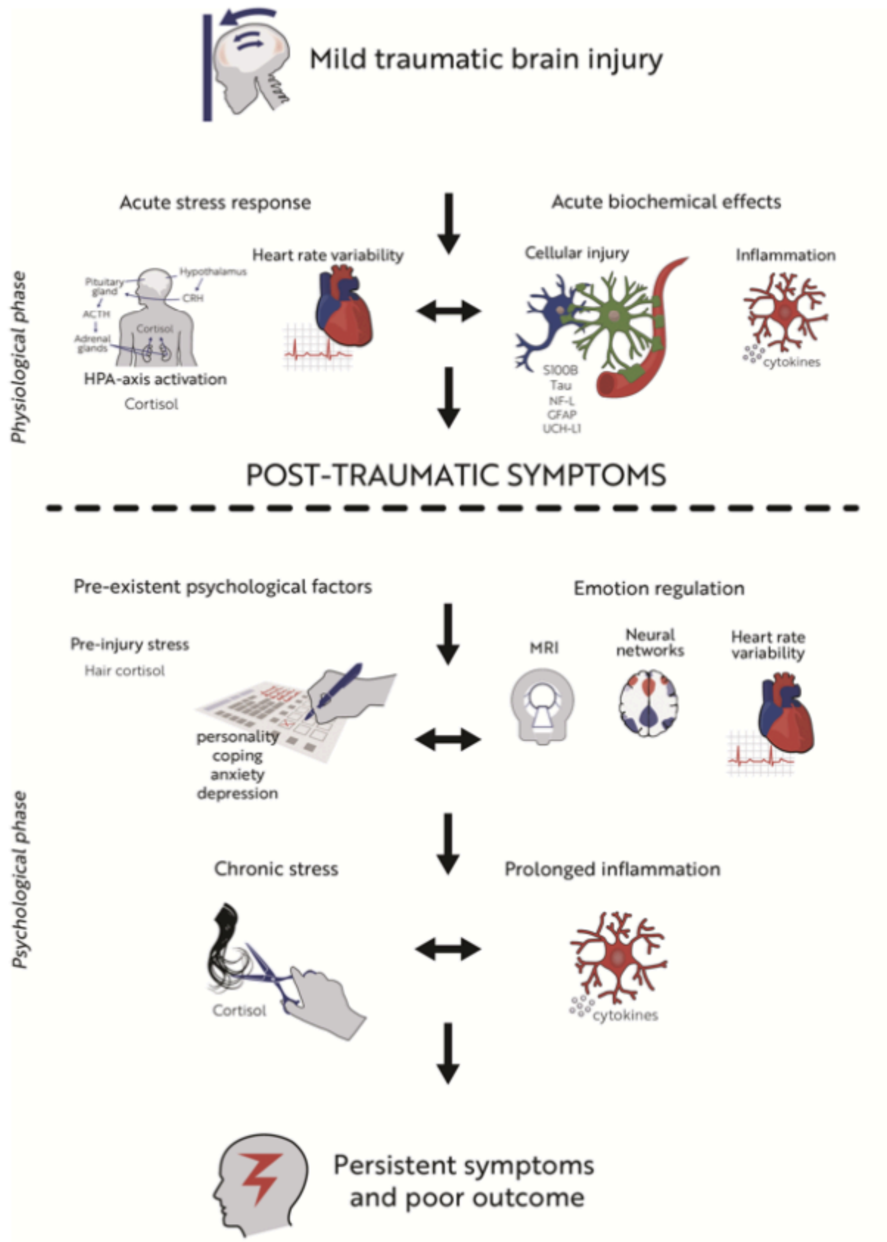

Figure 18 : Schématisation de différents facteurs et leur interaction expliquant l'étiologie des symptômes persistants. Note. Tiré de « An integrated perspective linking physiological and psychological consequences of mild traumatic brain injury », by van der Horn, H. J., 2019, Journal of neurology, 1-10, Copyright 2019 Infographics by Rikkert Veltman Media Productie