

Long-Term Cognitive Impairments of Sports Concussions in College-Aged Athletes: A Meta-Analysis

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ABSTRACT

Introduction/Purpose: This meta-analysis aimed to investigate the long-term (3+ months) consequences of concussion across cognitive domains (processing speed, memory, attention, and executive functions) and subdomains in young adult athletes (university, professional, or recreational). **Methods:** Six databases (EMBASE, PubMed, PsycINFO, SPORTDiscus, Web of Science, and Cochrane List of Registered Trials) were searched for studies that compared cognitive performance between athletes with a history of concussion (HOC) and control athletes who never sustained a brain injury. Thus, the analyses were restricted to the studies investigating sports concussions. **Results:** Nineteen studies, including 20 independent experiments with 1514 participants (521 HOC athletes, 1184 controls), were identified. Athletes from the HOC group sustained an average of 2.40 ± 0.99 concussions, with an average of 29.88 ± 19.26 months after injury. Importantly, all HOC athletes were tested at least 3 months after their most recent concussion. The results indicated significant medium-to-large group differences (Hedges' $g = 0.55-1.03$; P values < 0.0001) for executive functions subdomains on both standardized clinical tests and screening tools. Specifically, HOC athletes had lower cognitive performance relative to controls in strategy generation/regulation, verbal set-shifting and interference management on standardized clinical tests (Regensburger verbal fluency S words and G/R words), and response inhibition (IMPACT Impulse Control composite) and prospective working memory (Cogstate two-back task) on screening tools. Encoding phase of visual memory (Brief Visuospatial Memory Test) on standardized clinical tests approached significance (Hedges' $g = 0.40$; P values = 0.08). **Conclusions:** The current findings provide a preliminary guideline to clinicians for the assessment of cognition in HOC athletes and inform future guidelines on common data elements of sport-related concussions.

INTRODUCTION

There is increased scientific interest in trying to understand the postacute and long-term consequences of sport-related concussions (SRC) on cognitive functioning. The Berlin consensus statement defined SRC as a mild traumatic brain injury (mTBI) by which biomechanical forces induce complex pathophysiological processes that result in the alteration of mental status, which may or may not be accompanied by a loss of consciousness (1,2). SRC manifests through a variety of somatic, cognitive, and affective symptoms that are self-reported by athletes. In addition to the symptoms, the presence of oculomotor, balance, and cognitive alterations are observed in the days after SRC (3–5).

Recovery was traditionally defined as the resolution of postconcussive symptoms, within 2 to 3 wk in adults, although some individuals may experience lingering symptoms (2,6). According to a recent systematic review, most studies consider athletes to be recovered once they are free of symptoms and cognitive impairments (5). A growing body of literature suggests that cognitive alterations in attention, memory, and execu-

tive functions (EF) outlast the postconcussion symptom recovery (7). A recent meta-analysis of cognitive functioning in retired professional athletes with a history of multiple SRC report long-term (10+ yr from most recent SRC) alterations in verbal memory (immediate and delayed recall) and attention (8). However, studies investigating the long-term outcomes of SRC in otherwise healthy and active young adult athletes yield conflicting results. Overall, they suggest a pattern of alterations that do not support generalized cognitive impairment, as athletes perform well on most tasks but show group differences on one or two measures, especially on those measuring higher-level cognition or EF. The absence of group differences between athletes with a history of concussion (HOC) and controls might indicate cognitive recovery, yet it could also be attributed to the lack of sensitivity of the tasks

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used, insufficient statistical power due to small sample sizes, or important interindividual differences in recovery.

Meta-analyses are particularly useful when studies show inconsistent findings, as they provide the necessary power to detect the subtle cognitive differences that may exist between athletes with and without an HOC. To the best of our knowledge, a single meta-analysis was conducted to investigate the long-term cognitive outcomes of concussions in adolescents and young adults (7). Their results show small, yet significant effect sizes for the retrieval phase of episodic memory and EF. Several methodological limitations must be taken into consideration when interpreting these findings. First, athletes with a history of multiple SRC were compared with athletes who sustained a single injury, with the absence of a true control group with no HOC. This may underestimate the effect of the injury because there is evidence that a single SRC may be sufficient to produce subtle, yet long-term cognitive alterations (9,10). Second, heterogeneity, assessed by the Q statistic, was high across most cognitive domains evaluated, which does not allow the summary effect to be accurately interpreted. This heterogeneity might arise from the combination of different cognitive measures that may not well represent the given construct in a cognitive domain. For example, EF was not divided into core functions but rather was evaluated as a single cognitive domain. Moreover, the measures were not separated by modality (verbal vs nonverbal visual), which may have lowered the homogeneity. Finally, the meta-analysis was conducted over a decade ago and did not include computerized measures, which are now prevalent in SRC assessment, highlighting the need for an updated meta-analysis.

As of today, healthcare professionals are still facing the challenge of choosing the most appropriate tools among the many options to aid in their decisions in assessing SRC and determining the impact of the injury across cognitive domains (standardized traditional paper-and-pencil neuropsychological tests and screening computerized tests). However, the available systematic reviews and meta-analyses do not provide clear guidelines as to which cognitive measures are the most useful for assessment HOC athletes. Accordingly, the purpose of the current meta-analysis was to investigate the impact of a history of SRC (one or more) across cognitive domains (processing speed, memory, attention, EF), subdomains, modalities (verbal vs nonverbal visual), and type of tests (standardized clinical tests vs screening computerized test) in college-aged athletes relative to control athletes who never sustained an SRC.

METHODS

The guidelines for Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA; [11]) were followed in the present meta-analysis (see Supplemental Content 1 for the chart, <http://links.lww.com/TJACSM/A152>).

Search Strategies

A formal search under the guidance of a university librarian was performed on the electronic databases EMBASE (1974–), PubMed (1977–), PsycINFO (1887–), SPORTDiscus (1892–), Web of Science (1950–), and Cochrane List of Registered Trials (1992–) through October 1, 2020. The keywords used corresponded to three concepts: concussion, cognition/neuropsychology, and athletes. In addition to the formal data collection, an informal search (i.e., not using a concept map

and predefined keywords) was conducted (see Supplemental Content 2, <http://links.lww.com/TJACSM/A153>, for details on the research strategies). The two search strategies (formal and informal) were used because the rigidity of the formal process might lead to some oversights. Furthermore, the reference sections of systematic reviews and meta-analysis on SRC and gray literature were examined to minimize the possibility of overlooking studies. References of relevant studies were manually searched.

Inclusion/Exclusion Criteria

Studies were included for analysis if they met the following criteria: (i) participants were athletes (university, professional, or recreational) aged 18–35 yr; (ii) participants did not receive a diagnosis of neurodevelopmental, neurological, or psychiatric disorder before their first SRC; (iii) participants from the HOC group had a history of one or more medically diagnosed or self-reported SRC that occurred during adulthood (≥ 18 yr of age); (iv) athletes were last tested more than 3 months since their last SRC (based on the recommendation of the SRC common data elements (CDE) working group; [12]); (v) athletes from the control group had to be free of an HOC; and (vi) cognitive measures had to include standardized clinical tests or screening computerized tests (also known as neurocognitive computerized assessment tool, e.g., ImPACT, Cogstate, ANAM, DANA, CNS Vital Signs). The studies were excluded if they (i) were not published in English or French; (ii) were case studies with < 10 participants, letters to editor, opinions/commentaries, reviews, or meta-analyses; and (iii) did not include the necessary data for analyses or if corresponding authors did not respond to our request for such data.

Data Extraction

After a predefined strategy, two researchers independently assessed eligibility. Sociodemographic data (number of participants, proportion of male athletes, mean age, type of controls (athletes vs nonathletes)) and cognitive test data (type of tests (standardized clinical tests vs screening tools), test names and measures, cognitive domains and subdomains, modality (verbal vs nonverbal visual vs nonverbal auditory), statistical values) were extracted for HOC and control athletes for each eligible study. Furthermore, the following data were also extracted for the HOC group (mean number of SRC, time since injury in months, type of diagnosis (medically diagnosed vs self-reported vs self-report of a medical diagnosis), definition, symptomatic status).

OUTCOME MEASURES

The outcome measures were scores on cognitive tests (i.e., reaction time, accuracy, or composite scores). Outcome measures were sorted into four cognitive domains (processing speed, attention, memory, and EF), based on contemporary models of cognitive functioning (13–16), and if applicable, they were further sorted into modalities (verbal, visual, and nonverbal auditory). See Table S1 in Supplemental Content 3, <http://links.lww.com/TJACSM/A154>, for details on the classification.

ASSESSMENT OF THE RISK OF BIAS

The Newcastle–Ottawa Quality Assessment Scale for Cohort Studies was used for the assessment of risk of bias (17). This scale assesses the quality over three domains (selection, comparability,

and outcome) on a 9-point system, with a greater number of points indicating a higher-quality study. In addition, because few randomized control trials were conducted in SRC populations and guidelines for the assessment of risk of bias for nonrandomized control trials are not established, we added the following concussion-focused quality criteria. Specifically, we attributed quality points (from 0 to 5) to each study, as follows:

- 1) Experimental design (e.g., cross-sectional, longitudinal, randomized controlled trial)
- 2) Use of a published definition of SRC
- 3) Screening for neurodevelopmental disorders (attention-deficit/hyperactivity disorder, learning disabilities, and other)
- 4) Optimal testing conditions (i.e., individual assessments, laboratory setting)
- 5) Controlling (statistically or sample matching) for age, sex, years of education, symptoms, and other confounding variables

Data Analysis

To respect the assumption of independence of scores in statistical analysis, whenever several tasks or measures assessing the same cognitive subdomain were reported within a study, two licensed clinical neuropsychologists determined the most appropriate measure for the given cognitive subdomain (see Table S2 in Supplemental Content 4 for details, <http://links.lww.com/TJACSM/A155>). Standardized clinical tests and screening tools were analyzed separately because of their different measurement scales. Similar to previous published meta-analyses, a minimum of two outcome measures per cognitive subdomain was required to generate the forest plot (18). Random-effects models were used because of heterogeneity across studies. Measurement scales were standardized so that lower scores reflected a poorer cognitive functioning. The standardized mean difference was calculated using Hedges' adjusted g with a 95% confidence interval. Between-study heterogeneity of effect sizes was assessed using the τ^2 , χ^2 , and I^2 statistics. The I^2 statistic describes the percentage of variation across studies that is due to heterogeneity rather than chance; hence, the higher I^2 , the more heterogeneity. Data were analyzed with Review Manager 5.4 (The Cochrane Collaboration, London, United Kingdom), with an $\alpha = 0.05$ for all subdomains.

RESULTS

Study Selection

Fig. 1 presents a flowchart of the inclusion process. The formal search strategy identified 7560 records (2990 duplicates removed), whereas the informal search identified 5297 records (1778 duplicates removed), resulting in 8089 records. Only 5.9% (477 records) were duplicates from both search strategies, indicating that the combination of these two research strategies was valuable. Thus, 7612 records were screened based on the title and abstract, with 7096 being excluded. Five hundred and sixteen full-text articles were assessed for eligibility, with 484 being excluded.

Additional studies were excluded to ensure homogeneity of the final sample. As such, eight studies including female athletes only or a minority of male athletes were excluded, as previous studies indicated that female athletes might perform differently

than male athletes on measures of cognitive functioning (19). Because of the small number of studies and their heterogeneity, the five studies that only included experimental tasks were also excluded. Thus, our final sample included 19 studies, producing 20 independent HOC groups and 19 control groups (references 20–39).

Study Characteristics

The pooled sample size was 1184 (90.8% males) for the control athletes and 521 (93.7% males) for HOC athletes. The average age was 21.82 ± 2.03 yr for controls and 21.98 ± 2.05 yr for HOC athletes. Some studies included more than one HOC group; thus, the group that was the most similar to that of other studies in terms of injury characteristics and demographics was included to conserve homogeneity (see Supplemental Content 4 for details, <http://links.lww.com/TJACSM/A155>). Athletes from the HOC group sustained an average of 2.40 ± 0.99 SRC, with an average time since injury of 29.88 ± 19.27 months (range_{average} 6.30–62.40 months). Importantly, all HOC athletes were tested at least 3 months after their most recent SRC. See Table 1 for the details on study characteristics.

Assessment of Risk of Bias

According to the Newcastle–Ottawa Quality Assessment Scale for Cohort Studies (17), the overall methodological quality of the included studies was good, with an average of 6.50 ± 1.15 (range, 5–8). Furthermore, according to our 5-point concussion-focused scale, the studies included had 4.00 ± 0.92 points on average (range, 2–5 points). One studies (5.0%) had two points, five (20.0%) had three points, seven (35.0%) had four points, and seven (35.0%) had five points.

Cognitive Functioning

Of the 19 meta-analyses conducted, three were significant (see Table 2 and Supplemental Content 5 for forest plots, <http://links.lww.com/TJACSM/A156>). Specifically, HOC athletes ($n = 37$) performed worse than controls ($n = 43$) on verbal set-shifting and interference management assessed by the Regensburger Word Fluency G/R condition, with a large effect size (Hedges' $g = -0.82$ (-1.28 to -0.36), $Z = 3.50$, $P = 0.0005$). Furthermore, HOC athletes ($n = 102$) performed worse than controls ($n = 117$) on response inhibition assessed with the ImpACT Impulse Control, with a large effect size for each of the six studies (Hedges' $g = -1.03$ (-1.31 to -0.75), $Z = 7.11$, $P < 0.0001$). Moreover, HOC athletes ($n = 120$) performed worse than controls ($n = 98$) on the prospective working memory subdomain assessed by the Cogstate two-back task in two studies, with a medium-to-large effect (Hedges' $g = -0.55$ (-0.82 to -0.27), $Z = 3.92$, $P < 0.0001$). Outcome measures for the three significant subdomains were found to be appropriately homogeneous ($\tau^2 = 0.00$; $\chi^2 \leq 0.50$, P values ≥ 0.64 ; $I^2 = 0\%$). No other group difference was found (Hedges' $g \leq -0.35$; $Z \leq 1.91$; P values ≥ 0.08 ; see Supplemental Content 5 for forest plots, <http://links.lww.com/TJACSM/A156>).

Because of the high heterogeneity within the strategy generation and regulation subdomain, a subgroup analysis was conducted, with COWAT and Regensburger S words. HOC athletes ($n = 37$) performed worse than controls ($n = 43$) on the Regensburger S words, with a medium-to-large effect size (Hedges' $g = -0.78$ (-1.24 to -0.32), $Z = 3.32$, $P = 0.0009$). No group differences were observed on the COWAT (Hedges'

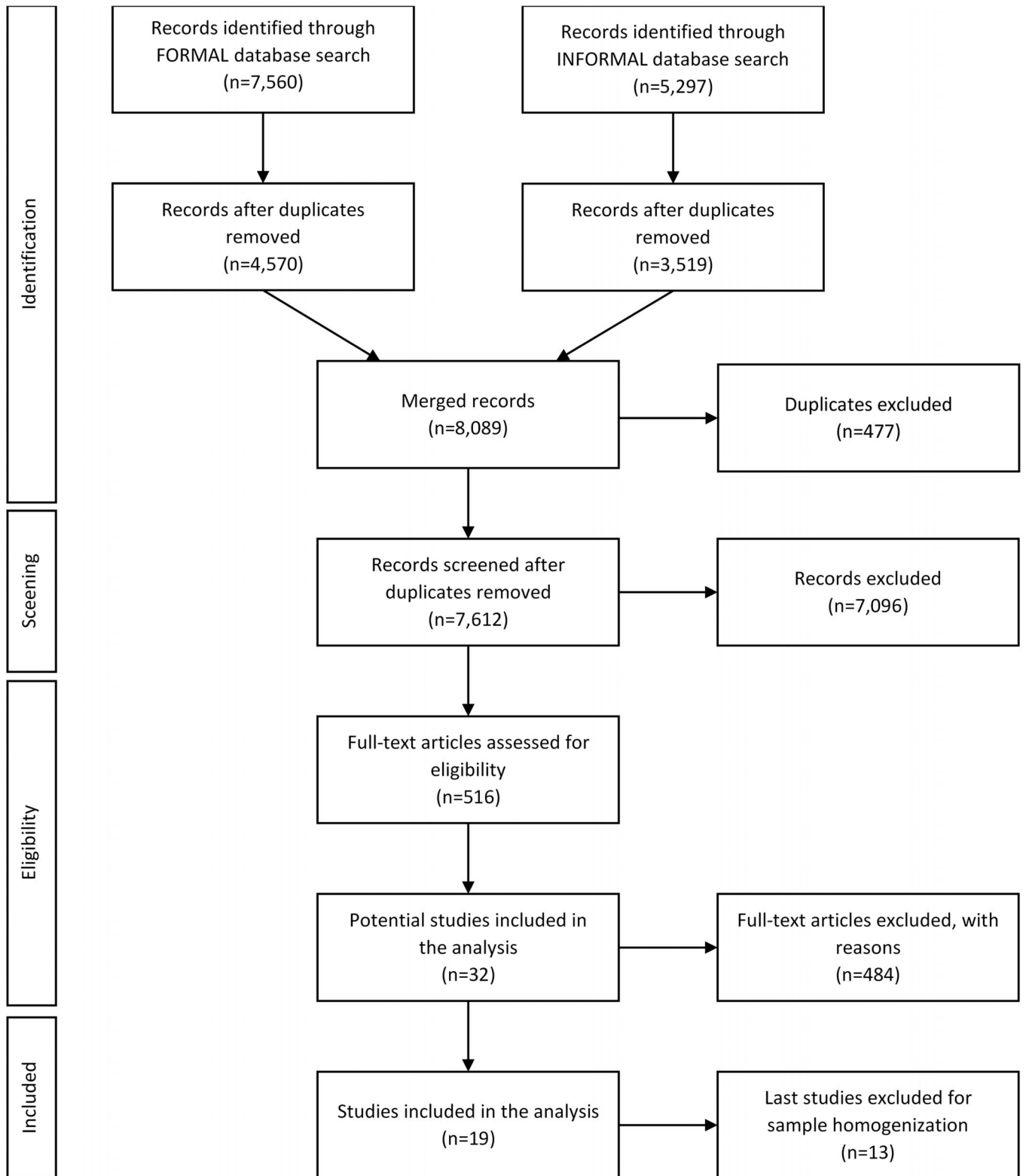


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of studies. One study included two independent samples.

$g = 0.13$ (-0.11 to 0.37), $Z = 1.03$, $P = 0.30$). By dividing the strategy generation and regulation subdomain as a function of the tests used, low heterogeneity was found ($\tau^2 = 0.00$; $\chi^2 \leq 4.70$, P values ≥ 0.45 ; $I^2 = 0\%$). Similar subgroup analyses

were conducted for visual set-shifting/interference management as an attempt to reduce heterogeneity. Specifically, Color Trails, standard Trail Making Test, and Delis-Kaplan Executive Function System Stroop switching were used as subgroups. No

TABLE 1.
Study Characteristics.

Studies	HC Characteristics				HOC Characteristics				Study Quality		
	<i>n</i>	% Males	Age (y), Mean (SD)	% Males	Age (y), Mean (SD)	No. Concussions, Mean (SD)	TSI (mo), Mean (SD)	Type ^a	Definition	5-Point Rating	NOSGEN
Baillargeon et al. (31)	15	100.0	23.40 (2.1)	15	100.0	23.30 (3.3)	6.30 (3.5)	1	CISG 3 rd + AAN	5	8
Broglio et al. (39)	18	ND	ND	173	ND	ND	≥6.00	2	Other	3	7
Broglio et al. (26)	44	59.6	19.40 (1.3)	46	84.9	20.00 (1.2)	40.80 (36.0)	3	ND	2	5
Bruce and Echemendia (24) ^b	292	100.0	19.32 (1.5)	42	100.0	20.04 (1.3)	≥6.00	2	AAN	3	5
Bruce and Echemendia (24) ^b	292	100.0	19.32 (1.5)	41	100.0	19.76 (1.9)	≥6.00	2	AAN	3	5
Clough et al. (28)	15	100.0	23.40 (1.4)	15	100.0	24.30 (3.3)	60.80 (9.6)	1	ND	3	7
De Beaumont et al. (22)	15	100.0	22.50 (2.5)	15	100.0	23.46 (2.7)	31.47 (22.3)	2	AAN	5	7
Gardner et al. (29)	39	100.0	23.90 (3.5)	34	100.0	22.79 (2.7)	18.39 (22.0)	2	WHO	5	6
Killam et al. (30)	9	66.7	22.00 (1.6)	6	50.0	21.80 (1.2)	62.40 (32.4)	3	AAN	4	6
Lavoie et al. (27)	10	100.0	21.40 (1.3)	10	100.0	21.60 (1.2)	9.75 (7.8)	2	ND	4	6
Leveille et al. (25)	15	100.0	21.44 (2.0)	10	100.0	21.59 (1.9)	24.14 (9.1)	2	CISG 4 th	5	5
List et al. (20)	21	90.5	25.70 (5.2)	20	90.0	25.50 (5.3)	25.50 (28.9)	2	AAN	4	7
Moore et al. (32)	16	100.0	22.25 (0.3)	14	100.0	23.36 (0.3)	27.30 (3.6)	1	CISG 3 rd + AAN	5	8
Pontifex et al. (33)	36	58.3	19.40 (1.4)	30	76.7	19.90 (1.2)	34.80 (34.8)	3	AAN	4	5
Pontifex et al. (34)	42	59.5	19.40 (1.3)	38	84.2	20.00 (1.3)	43.20 (38.4)	1	AAN	4	6
Sicard et al. (21)	49	100.0	21.55 (1.4)	49	100.0	21.53 (1.6)	24.92 (16.1)	1	CISG 3 rd	5	8
Sicard et al. (35)	49	100.0	21.55 (1.8)	71	100.0	21.30 (1.5)	24.18 (15.3)	1	CISG 3 rd	5	8
Terry et al. (36)	20	100.0	20.40 (1.6)	20	100.0	20.30 (1.2)	19.60 (18.9)	2	ACRM	4	7
Theriault et al. (23)	10	100.0	22.10 (1.4)	10	100.0	22.90 (3.3)	33.20 (15.4)	2	ND	3	6
Wilke et al. (38)	22	90.9	26.10 (5.4)	17	88.2	24.20 (2.8)	21.20 (13.5)	2	AAN	4	8

AAN, American Academy of Neurology; ACRM, American Congress of Rehabilitation Medicine; CISG, Concussion in Sports Group; HC, healthy control athletes; ND, no data; NOSGEN, Newcastle–Ottawa Quality Assessment Scale for Cohort Studies; TSI, time since injury; WHO, World Health Organization.

^a Type of concussion: 1, medically diagnosed; 2, self-reported HOCs; 3, self-reported history of diagnosed concussions; 4, self-reported HOCs, but the most recent concussion was diagnosed.

^b Bruce and Echemendia (24) included two experiments with independent samples, one used screening tools only and the other used standard clinical tests only.

TABLE 2.
Meta-Analyses of Cognitive Domains for Standardized Clinical Tests and Screening Tools.

Cognitive Domains/Subdomains	Studies, <i>n</i>	HOC, <i>n</i>	Control, <i>n</i>	SMD	Lower	Upper	<i>r</i> ²	<i>χ</i> ²	<i>I</i> ² (%)	<i>P</i>
Standardized clinical tests										
Processing speed	13	233	493	-0.05	-0.24	0.14	0.01	13.61	12	0.61
Selective attention	4	50	50	-0.17	-0.56	0.23	0.00	0.35	0	0.41
Verbal memory—encoding	11	178	445	0.01	-0.20	0.23	0.02	11.69	14	0.90
Visual memory—encoding	3	40	40	-0.40	-0.84	0.05	0.00	0.68	0	0.08
Verbal memory—retrieval	10	164	429	-0.12	-0.32	0.07	0.00	5.50	0	0.21
Visual memory—retrieval	3	40	40	-0.09	-0.55	0.37	0.01	2.12	6	0.70
EF—prospective working memory	5	87	93	-0.13	-0.43	0.16	0.00	2.97	0	0.38
EF—response inhibition	6	106	367	0.11	-0.12	0.35	0.00	2.78	0	0.35
EF—verbal set-shifting/interference management	2	37	43	-0.82	-1.28	-0.36	0.00	0.00	0	0.0005
EF—visual set-shifting/interference management	6	101	357	0.14	-0.23	0.51	0.09	8.76	43	0.44
EF—strategy generation/regulation	7	138	400	-0.19	-0.56	0.17	0.15	16.73	58	0.29
Screening tools										
Processing speed—reaction time	8	328	884	0.00	-0.25	0.25	0.09	22.03	68	1.00
Processing speed—visual motor speed	6	208	626	-0.17	-0.38	0.04	0.02	7.19	30	0.11
Sustained attention	2	120	98	0.20	-0.07	0.47	0.00	0.04	0	0.15
Verbal memory—storage	6	208	626	0.07	-0.10	0.25	0.00	0.43	0	0.40
Visual memory—storage	5	166	334	-0.15	-0.35	0.06	0.00	1.62	0	0.16
Visual memory—encoding	2	120	98	0.13	-0.13	0.40	0.00	0.02	0	0.33
EF—response inhibition	3	102	117	-1.03	-1.31	-0.75	0.00	0.50	0	<0.0001
EF—prospective working memory	2	120	98	-0.55	-0.82	-0.27	0.00	0.21	0	<0.0001

Significant analyses are denoted by a bold font.
SMD, standard mean difference.

subgroup was significant (P values ≥ 0.09), and heterogeneity within Color Trails B subgroup was still high ($I^2 = 26\%$).

It is interesting to note that the encoding phase of visual memory, assessed by the Brief Visuospatial Memory Test in all three studies included, approached significance (Hedges' $g = -0.40$ (-0.84 to 0.05), $Z = 1.75$, $P = 0.08$), with HOC athletes ($n = 40$) performing worse than controls ($n = 40$).

DISCUSSION

This meta-analysis aimed to investigate the long-term consequences of SRC across cognitive domains and subdomains in college-aged male athletes relative to controls who never sustained an SRC. Accordingly, separate forest plots were generated per type of test (standardized clinical tests and screening tests), cognitive domains (processing speed, attention, episodic memory, and EF) and subdomains, and per modality (visual, verbal, and auditory nonverbal), when applicable. Overall, three analyses were significant: verbal set-shifting and interference management on standardized clinical tests, as well as prospective working memory and response inhibition on screening tools. The current results suggest that tasks tapping into EF might be more sensitive to long-term alterations of SRC.

Both the letter fluency condition (simple words in S) and letter switching condition (words in G/R) of the Regensburger Verbal Fluency Test can discriminate between HOC athletes and controls, with the HOC athletes performing significantly worse. It is worth noting that the two studies included in these analyses are from the same research group, limiting the generalization of these findings. Nevertheless, these results are consistent with those of previous mTBI studies (40–42). For example, mTBI patients on average of 1.5 yr after injury admitted to a trauma center generated fewer words relative to demographically similar controls (40). Furthermore, prior studies suggest that letter fluency tests should be privileged over semantic fluency tests (41–43), as generating words from a given letter is considered to solicit more prefrontal functions (i.e., EF), which are thought to be more vulnerable to concussive injuries. Overall, the current results support the use of the Regensburger Verbal Fluency Test for the examination of EF in HOC athletes.

Although standardized clinical tests did not show a group difference in prospective working memory and response inhibition, HOC athletes exhibited a lower response accuracy relative to controls on the two-back condition of the Cogstate and on the ImPACT Impulse Control composite. These results are in line with a growing body of literature showing alterations in brain activation in regions underlying working memory and response inhibition. Indeed, most working memory studies of concussion have used an N -back paradigm (44–49), which requires the upregulation and co-ordination of sustained attention, working memory, and cognitive inhibition to correctly detect and correctly reject target and nontarget stimuli, respectively (50). The N -back task, especially the two-back condition due to its higher cognitive load in working memory, might be more sensitive to the long-term consequences of SRC relative to the paper-and-pencil tests such as the Operation Span, Digit Span Backwards, Brown–Peterson, and Letter–Number Sequencing tests, as it involves the updating component of working memory. It is important to note that the two studies included in the analyses herein came from the same research group and used raw scores instead of the automated clinical output variables. Indeed, the Cogstate program autotransforms data under the assumption

that they are abnormally distributed. As highlighted by two studies from Sicard and colleagues (21,35), the raw scores accurately discriminated between HOC athletes and controls, whereas the clinical output variables did not.

The ImPACT Impulse Control composite score could also distinguish between HOC athletes and controls, with HOC athletes performing worse. These results are consistent with neuroimaging and electrophysiology studies of mTBI and SRC using experimental tasks of response inhibition, such as the Flanker, Stop Signal, and Go/No-Go tasks (51–58). However, two studies using the ImPACT battery to investigate the consequences of SRC beyond the acute phase of injury have not found a difference on the ImPACT Impulse Control (59,60). These two studies could not be included in the current meta-analysis as their time because injury was highly variable and did not distinguish between the different phases of injury, and their exclusion highlights the need for studies to use clear definition of acute, subacute, and chronic/long-term phases of injury. Future studies should use the recently published guidelines of the SRC CDE working group to define the phases of injury (12). Indeed, 32 worldwide experts in concussion from varied field divided the postinjury period into three subgroups: acute (≤ 72 h), subacute (3 d–3 months), and persistent/chronic/long-term (>3 months).

Our findings are, at least in part, consistent with those from a previous meta-analysis (7). Both the previous study and the current meta-analysis observed long-term alterations of EF. However, the former observed group differences in the retrieval phase of memory, whereas no memory analyses were significant herein. Methodological differences between the previous study and ours are worth noting, as they could explain some of the discrepancies. The former compared athletes who sustained multiple SRC with athletes who sustained a single injury, considered EF as a single construct, did not analyze verbal and visual tasks separately, and included only standardized clinical measures. Thus, the present meta-analysis extends on the previously published meta-analysis by dividing EF into subdomains, disambiguating verbal and nonverbal visual processes, and incorporating screening tools, which have become increasingly implemented over the last decade.

Most cognitive subdomains did not show significant differences; however, that does not mean that SRC do not have a long-lasting impact on cognition. Indeed, it has been proposed that HOC athletes could perform normally on standardized clinical tests and screening tools because of compensatory mechanisms (10). This is supported by the results of several studies that provide evidence for neurophysiological alterations underlying certain cognitive processes in the absence of impaired performances on standardized clinical tests or screening tools (9, 27,31,37). Furthermore, recent studies in pediatric (61,62) and adult populations (63,64) indicate that, although most athletes will recover within a month after injury, a subgroup of concussed individuals exhibit cognitive deficits that persist months after the injury. The important heterogeneity in the clinical profile of concussion/mTBI can be hidden within the group means and might contribute to null results. Thus, clinicians and researchers need to be cognizant of this interindividual variability when interpreting the current findings.

It is also possible that the results of the present meta-analysis do generalize to a nonathlete population. It should be taken into consideration that college-level athletes may have better cognitive abilities relative to healthy, yet sedentary young adults, as

accumulating evidence suggests that regular physical activity has beneficial effects on cognitive functioning (65). This could favor athletes during cognitive testing; hence, researchers and clinicians should maximize their chance to detect cognitive impairments in an athlete population by adding more challenging conditions to their cognitive test batteries or by adding physical stress. For example, two of the included studies added a two-back condition to the core Cogstate battery to increase the cognitive load in working and only observed group differences on this task (21,35). Moreover, other studies found that athletes who did not present cognitive alterations at rest exhibited alterations after an acute bout of moderate exercise (66,67), which can be reflective of incomplete neurophysiological recovery.

The current meta-analysis is limited by the measures included in the published articles and, as such, may suffer from a lack of construct invalidity due to task/composite score impurity. For example, the ImpACT battery generates a composite score for impulse control, which is the sum of errors on two tasks measuring different aspects of inhibition. This is particularly relevant as recent studies using experimental paradigms of EF suggest that different forms of inhibition and cognitive flexibility have differential recovery trajectories (68). Thus, despite our effort to divide EF into core functions, this was dependent on the manner in which outcome measures are calculated by test providers.

Experimental paradigms, that is, cognitive tests that are not commercially available and most likely have not been formally psychometrically validated, were excluded from the present analyses. This decision was twofold: first, we wanted to preserve homogeneity; second, we endeavored to provide insight regarding the tools that are readily available and currently used in the clinical assessment of concussion. However, it is important to note that a growing body of literature suggests that long-term alterations may be observed using experimental cognitive paradigms several months to years after a concussion. Those alterations seem to be specific to the aspects of EF, such as cognitive flexibility, working memory, and inhibition and interference control (22,26,27,32,33,44,51,52,54,64,68–76). Together with previous studies, the current findings reinforce the need for the development and validation of more sophisticated tests of complex cognitive processes to measure deficits that persist after a concussion.

Although some might argue that the currently observed alterations are mild and likely of minimal clinical significance, the assessment of everyday functioning is required to confirm such an assertion, which should be taken into consideration in future studies. Regardless of whether these alterations are clinically significant at this point in the athletes' lives, they may place HOC athletes at a greater risk of incurring additional concussions, and as highlighted by a recent meta-analysis in retired athletes (8), they could eventually evolve into more clinically significant cognitive dysfunctions later in life.

Limitations

Although the current findings advance the understanding of the nature and the duration of concussion-related alterations on cognitive functioning, they must be interpreted considering the limitations imposed by the literature. The present meta-analysis used strict eligibility criteria to avoid the effect of confounds on the findings; however, it may limit the generalization of findings. For example, studies in the present meta-analysis included a majority of not only male athletes. The little that is

known about SRC in female athletes indicates that they are more at risk of sustaining a concussive injury and of exhibiting longer recovery (77–79). As such, our results can only be extended to male athletes. It is important for studies examining the neuropsychological outcomes of SRC to assess/measure and control for the plethora of potential confounding variables that were identified in the literature, such as premorbid intelligence, symptomatology, learning disabilities/attention-deficit/hyperactivity disorder, and number of previous SRC. The time since the last injury is highly heterogeneous (29.88 ± 19.26 months; range_{average}, 6.30–62.40 months), limiting the understanding of long-term cognitive alterations as several uncontrolled factors and life events can have an impact on the recovery. Furthermore, most studies relied upon self-reported HOC or the self-reported diagnosis of SRC rather than medical records. Although this was necessary as medical records are seldom available to research teams and athletes do not necessarily seek medical help after their injury (80,81), it likely introduces biases due to errors in retrospective memory, leading to either underestimation or overestimation of the number of SRC sustained (8). Finally, statistical test was performed to control for publication bias, although it was minimized through the combination of formal and informal research strategies, as well as research in the gray literature.

Conclusions and Future Directions

The present meta-analysis indicated that HOC athletes show a lower performance on standardized clinical tasks of visual set-shifting and interference management. Furthermore, a group difference was observed in response inhibition and prospective working memory on screening tools. Importantly, all group differences observed herein were on tasks of EF, suggesting that concussion assessment should include measures of EF. Encoding in visual memory on standardized clinical tests also approached significance, which warrants further investigation. Additional studies are needed to identify the readily available cognitive tests that should be included in the SRC assessment, as the early detection of athletes who exhibit long-term cognitive alterations may help preemptively manage their condition.

To better understand the long-term consequences of concussions on cognitive functioning, original research need to 1) divide findings by phases of injury (e.g., acute, subacute, chronic, late chronic, such as presented in the CDE recommendations (12); 2) analyze female and male athletes separately; 3) analyze data from children, adolescents, and adults separately; 4) control for learning disorders; and 5) better describe the samples in terms of demographic information (e.g., socioeconomic status, presence of neuropsychiatric disorders, premorbid cognitive abilities) and concussion information (e.g., previous HOC and symptom duration, definition used, presence of ongoing symptoms).

In closing, the current research will serve as an impetus for increased research efforts in clinic settings and in the laboratory and may facilitate the assessment and management of SRC by informing future CDE guidelines (12,60,82).

Fanny Redlinger and Veronik Sicard have contributed equally to the manuscript.

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