Corlùy *et al. Sports Medicine - Open* (2026) 12:17
https://doi.org/10.1186/s40798-025-00951-5

Sports Medicine - Open

SYSTEMATIC REVIEW Open Access

Neurocognitive Deficits Related to Ligamentous Ankle Injuries: A Systematic Review

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Abstract

Background Lateral ankle sprains (LAS) are among the most common sports injuries, with up to 40% of individuals developing chronic ankle instability (CAI). While altering neurocognitive demands can affect lower limb biomechanics, the underlying mechanisms in CAI patients remain unclear. This systematic review aimed to summarise evidence on the neurocognitive deficits linked with ligamentous ankle injuries and CAI.

Methods Following PRISMA guidelines (PROSPERO: CRD42023406395), a comprehensive search of five databases (up to September 24, 2024) identified studies examining neurocognitive performance in adults with LAS or CAI. Inclusion criteria were based on a PICO strategy. Two authors independently selected studies and assessed bias using the QUIPS tool and the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. Data were extracted using a standardized form detailing study characteristics, patient data, neurocognitive methods, and statistical outcomes.

Results This review included 24 studies with 104 LAS and 393 CAI patients, 92 copers, and 317 healthy controls. Eighty-three percent of the included studies showed a high risk of bias. Neurocognitive performance was assessed across nine domains using 27 neurocognitive tasks. CAI patients exhibit deficits in attention, inhibitory control, and visual memory, with mixed results for working memory and processing speed. No deficits were found in language or motor skills. These deficits may contribute to reduced postural stability, particularly under dual-task conditions where cognitive resources are divided. No significant findings were observed for copers.

Discussion Methodological variability, cross-sectional designs, and limited focus on LAS underscore the need for further research to examine causality and expand generalizability.

Conclusion This review underscores the association between ligamentous ankle injuries, particularly in CAI, and neurocognitive performance, although more research is needed to unravel the causal direction.

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Key Points

1. Patients with chronic ankle instability exhibit deficits in attention, inhibitory control and visual memory compared to healthy controls and copers.
2. Longitudinal studies are necessary to determine whether neurocognitive deficits arise as a consequence of ankle injuries or whether they pre-exist and contribute to injury occurrence.
3. Integrating neurocognitive considerations, such as dual-task training, into rehabilitation programs may help address deficits in attention, inhibitory control, and visual memory. While this approach holds promise, further research is needed to determine its effectiveness and added value compared to traditional rehabilitation methods.

Keywords Injury risk, Postural control, Cognition, Performance, Brain, Chronic ankle instability

Introduction

The ankle is the most commonly injured body part in sports, with lateral ankle sprain (LAS) being the most prevalent ankle injury, affecting athletes of all levels [1]. Ankle sprain incidence in the general population has been reported to range from 19.0 to 26.6 per 1000 person-years [1, 2], with up to 40% of individuals who experience an initial LAS progressing to chronic ankle instability (CAI) [2, 3]. This condition is characterized by recurrent sprains, persistent pain, and disability [4]. CAI has also been linked to a higher risk of early-onset osteoarthritis [5], and decreased physical activity levels [6], affecting an individual's long-term health and quality of life [7]. Given the high prevalence and substantial burden of ligamentous ankle injuries, understanding the mechanisms behind LAS and CAI is crucial for improving prevention and treatment strategies.

While the peripheral and mechanical aspects of ankle injuries have been extensively studied, emerging research suggests that LAS and CAI may involve more than just ligamentous and structural damage. Hertel et al. (2019) [8] proposed a paradigm to describe the current understanding of the pathophysiology of CAI. The authors describe how a primary tissue injury to the lateral ankle ligaments from an acute LAS may lead to interrelated pathomechanics, sensory-perceptual, and motor-behavioural deficits that influence a patient's clinical outcome [8]. Recent literature [9] brings attention to the complexity of ligamentous ankle injuries by exploring their impact on the brain and neurocognitive processes. This complexity is also brought to attention in a recent systematic review demonstrating that individuals with LAS and CAI exhibit unfavourable structural and functional adaptations in the brain compared to healthy individuals or copers [10]. These adaptations are associated with poor clinical outcomes, such as lower self-reported function, postural control and dual-tasking [10]. Based on these findings, neurocognition could likely play a role in the occurrence of ankle sprains, as well as the development and persistence of CAI. By contrast, the role of neurocognition often remains underemphasized in research and clinical practice.

Recent studies have demonstrated that neurocognitive performance impacts an athlete's ability to perceive and respond to external forces, particularly in movements with high risk for ankle injuries, including jumping, cutting, and lateral movements in sports such as basketball, soccer, and volleyball [11]. The time required for visual perception, information processing, and generating a motor response may be crucial for maintaining situational awareness and minimizing the risk of injury during athletic activities [12]. Therefore, understanding the relationship between neurocognitive performance and injury risk is critical for developing effective sports injury prevention and management strategies. This relationship has already been observed in ACL injuries, where deficits in baseline neurocognitive performance are associated with an increased risk of injury during cognitively challenging movements [13]. Additionally, cross-sectional studies have discovered biomechanical patterns associated with an elevated risk of injury in individuals with worse neurocognitive performance [14–18]. A similar relationship may exist in LAS and CAI, where deficits in neurocognitive performance could impair an athlete's ability to appropriately respond to external stimuli, potentially increasing the likelihood of (re)injury. However, the link between neurocognition and ankle injuries has received far less attention in the literature compared to other musculoskeletal injuries.

Accordingly, the aim of this review is threefold. First, this review aims to summarise the literature on the relationship between neurocognitive impairments and ankle injury risk. Second, the review aims to investigate if neurocognition is affected following lateral ligamentous ankle injuries. The final aim is to investigate the differences in neurocognition between healthy individuals and individuals with LAS or CAI. This review will provide insight into the role of neurocognition in ligamentous ankle injuries and highlight its potential role in rehabilitation, injury screening and return-to-sport decision-making.

Methods

The present systematic review was conducted following the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) [19]. The review protocol was recorded in the International Prospective Register of Systematic Reviews (PROSPERO—CRD42023406395).

Information Sources and Search Strategy

A comprehensive literature search was conducted using five electronic databases, including MEDLINE (via PubMed), Web of Science Core collection (via Clarivate), Scopus (via Elsevier), PsycINFO (via ProQuest) and SPORTDiscus (via EBSCOhost) from their dates of inception to September 24th, 2024. Grey literature was not included in this review, as the focus was on peer-reviewed, published research to guarantee methodological rigor and data quality. The search strategy was developed based on a combination of relevant keywords and medical subject headings using the PICO framework to identify terms related to our research questions. The type of injury (1) and outcomes of interest (2) were combined using the "AND" boolean operator. Each term within these categories was combined using the "OR" boolean operator. No filters were applied. The search strategy is summarised in Table 1.

Eligibility Criteria

Articles were eligible if they (1) investigated neurocognitive performance in 18-year-old or older individuals with CAI or who experienced a LAS, (2) were original research, and (3) were published in English, Dutch or French. Studies investigating other injuries or not investigating neurocognitive performance were excluded. Neurocognition refers to the cognitive processes and abilities associated with the functioning of both cortical and subcortical brain systems, encompassing domains such as attention, processing speed, and motor skills control [20, 21]. Neurocognitive tasks, which assess reaction time, processing speed, and memory, serve as indirect measures of cerebral performance [21]. While it also includes broader functions like language and intelligence, key aspects relevant to injury risk include visual attention, self-monitoring, fine motor performance, and dual-tasking abilities [16]. The definitions used for CAI, LAS and copers were recommended by the International Ankle Consortium [4]. LAS is defined in accordance with Gribble et al. (2013) [4] as "an acute traumatic injury to the lateral ligament complex of the ankle joint as a result of excessive inversion of the rear foot or a combined plantar flexion and adduction of the foot. This usually results in some initial deficits of function and disability". To be considered CAI, individuals must have a history of at least 1 significant ankle sprain and a history of the previously injured ankle joint "giving way," and/or recurrent sprain, and/or "feelings of instability". To qualify as a coper, individuals must have a history of one significant ankle sprain without symptoms of "giving way", and/or recurrent sprain, and/or "feelings of instability". Finally, control participants are defined as individuals with no history of LAS or related symptoms, and who exhibit stable ankle function without any signs of instability.

Study Selection Process

The study selection process consisted of two stages. Firstly, all retrieved studies were imported into Rayyan's web application [22] and duplicates were detected by Rayyan and manually reviewed by two authors (H.C. and E.S.). The same two authors independently conducted initial screenings of the articles based on their titles and abstracts. Subsequently, they evaluated the remaining articles in full text to determine their eligibility. The authors contacted the authors of studies for which the full text was not initially available to obtain this. In cases of conflicts between the two authors, a third author (A.M.) was contacted to resolve the conflicts. Any discrepancies between the authors were resolved through discussion to reach consensus.

Study Risk of Bias Assessment

All included articles were independently assessed for any potential bias by two authors (H.C. and E.S.) using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies form and the Quality in Prognostic Studies (QUIPS) tool. For the assessment of the cross-sectional studies, 14 criteria are used to determine

Table 1 Search strategy

1.	*((ankle injur*) OR (ankle sprain) OR ("lateral ankle sprain") OR ("ankle inversion trauma") OR (chronic ankle instability))*
2.	*(("cognition"[Mesh]) OR (neurocogniti*) OR (neural mechanism*) OR (neural consequences) OR (Neuroscience application) OR (neuroscience*) OR (cognitive performance) OR cogniti* OR "cognitive function*")*
3.	*#1 AND #2*

the risk of bias with "yes", "not reported / not applicable / can't decide" and "no" answers. Additionally, QUIPS considers eight important domains to judge the level of bias of the included studies. To identify the overall bias, we assigned equal weighted scores to each criterion. The accumulation of scores yielded a total score expressed as a percentage. Each criterion received a score based on the level of bias risk: a low risk of bias received two points, a "not applicable" answer was given one point, and a high risk, unclear or "not reported" answer received zero points. The scores for each criterion were then added up to calculate a total score expressed as a percentage. Studies with a total score between 75 and 100% were considered to have a low risk of bias, while those scoring less than 55% indicated a high risk of bias. Studies scoring between 55 and 75% were considered to have a fair risk of bias. In cases of any disagreements in risk of bias scores, resolution was achieved through discussion.

Data Extraction Process and Synthesis Method

Data were extracted by two authors (H.C. and E.S.) using a standardised data extraction form. The following information was extracted: (1) study characteristics (authors' names, publication year and study design), (2) in- and exclusion criteria, (3) patient characteristics (sample size, age, sex, and clinical characteristics), (4) methods used to assess neurocognitive performance, (5) associated outcome measures and (6) all statistical analyses of primary and secondary neurocognitive outcomes. The primary outcome measures of neurocognition included change-from-baseline measures of cognitive tasks. The outcome measures were assessed by reporting the means and standard deviations of the continuous variables in each study. Statistical differences were considered to be present between the groups if the p-value was lower than 0.05. Secondary outcomes were functional outcomes (e.g. stability, foot and leg kinematics) related to the primary neurocognitive outcome of interest. The results of the included studies were synthesised using a narrative synthesis approach. To create a better overview of the different populations, individuals with CAI, copers who experienced an initial LAS and control participants without a history of LAS were considered as distinct groups. A meta-analysis was not possible due to the heterogeneity of the included studies.

Results

Search Results

A total of twenty-four studies met the inclusion criteria of this systematic review [23–46]. The overview of the selection process is provided in Fig. 1. The twenty-four included studies encompassed a total of 104 individuals with LAS across four studies [36, 41, 45, 46], 393 individuals with CAI across 20 studies [23–35, 37–40, 42–44], 317 healthy controls across seventeen studies [24–28, 30–33, 36, 38–40, 42–44, 46], and 92 copers across six studies [25, 27, 32, 33, 42, 45].

Risk of Bias Assessment

Overall Risk of Bias

The risk of bias assessment revealed an overall high risk of bias. All included articles were cross-sectional studies [23–28, 30–44, 46] except two prospective studies [29, 45]. Out of the twenty-two cross-sectional studies, twenty were labelled with a high risk of bias, while the remaining two cross-sectional studies [37, 39] as well as the two prospective studies were considered to have a fair risk of bias [29, 45].

Sources of Bias for the Cross-Sectional Studies

Five articles out of twenty-two had a high risk of bias for study population due to unclear demographic information [23, 24, 26, 35, 38]. Twenty articles were at a high risk of bias for participation rate because less than 50% of eligible individuals participated or participation rate was not reported [23–28, 30–34, 36–44]. Fourteen studies were labelled as high risk of bias for inadequate sample size because there was no sample size justification reported [23–25, 27, 28, 31–33, 35, 36, 38, 40, 42, 46]. All studies had a high risk for exposure prior to outcome and timeframe. This is typical for cross-sectional studies since the exposures and outcomes are measured during the same timeframe. Five studies measured different levels of exposure, limiting the risk of bias [31, 35, 37, 42, 46]. All articles, except two [27, 43], were labelled as high risk of bias for not reporting blinded outcome assessors, and twenty-one were high risk for not implementing or reporting follow-up rates [23–28, 30–38, 40–44, 46]. Finally, twenty articles were high risk for not correcting for confounding variables [23–28, 30–43].

Sources of Bias for the Prospective Studies

The prospective studies were considered to have a fair risk of bias for study participation and prognostic factor measurement. Study attrition was labelled as high risk of bias and confounding was labelled as high risk of bias for one study [29] and fair risk of bias for the other [47], while outcome measurement and statistical analysis were detected as low risk. Figures 2, 3, 4, 5 provide an overview of the risk of bias.

Neurocognitive Deficits Related to Injury or Reinjury Outcomes

None of the studies included in this review directly evaluated injury or reinjury outcomes in relation to neurocognitive deficits. As such, while this remains a plausible hypothesis, current evidence does not allow conclusions

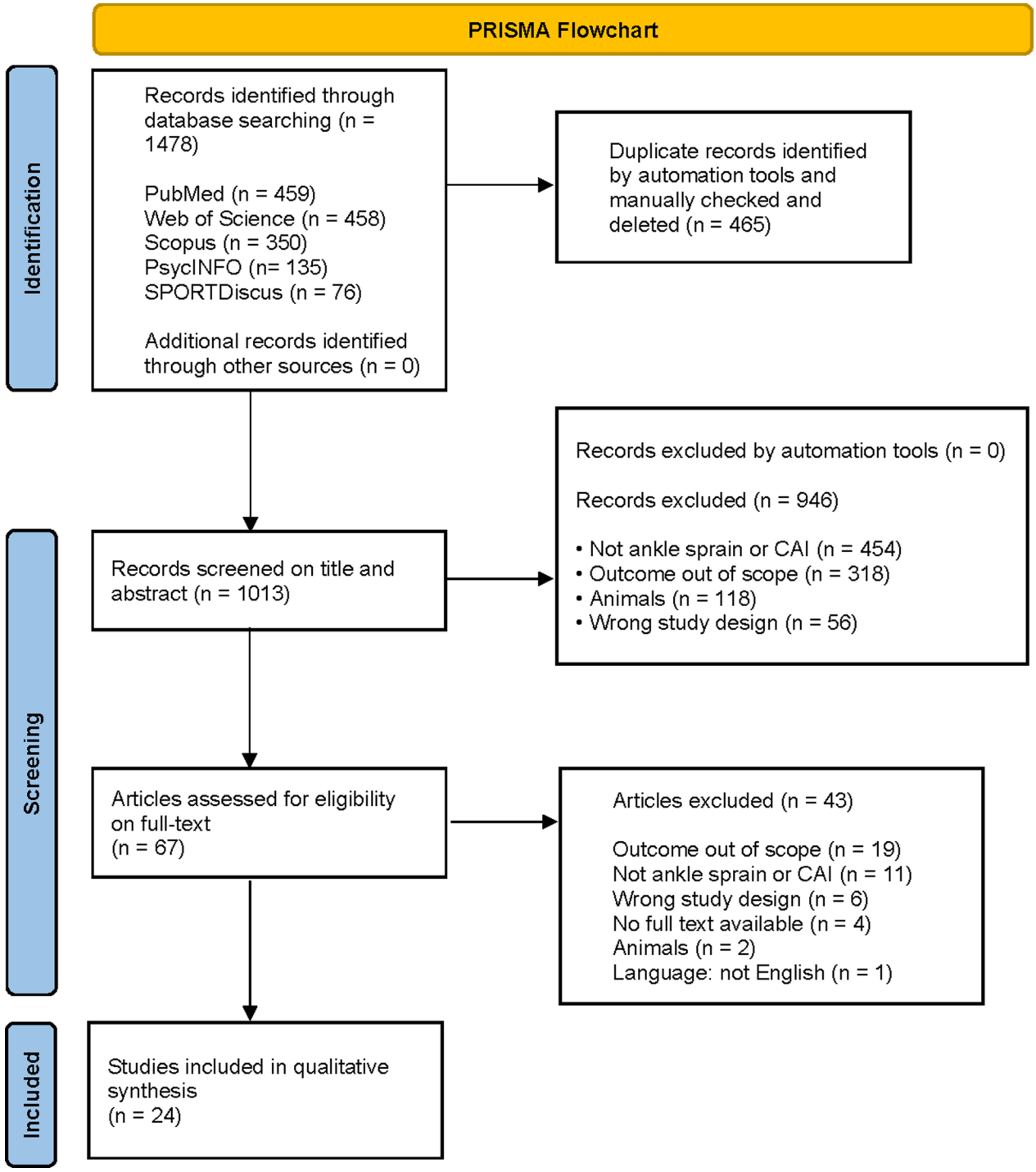

Fig. 1 Selection process of the included studies using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart [19]

regarding the role of neurocognition in the risk of initial or recurrent ankle injury.

Neurocognitive Domains Related to Ligamentous Ankle Injuries and CAI

The included studies employed 27 cognitive tasks to assess different neurocognitive domains associated with ligamentous ankle injuries. These tasks were designed to target specific cognitive functions. Nine key cognitive domains were identified across the included studies to evaluate the relationship between neurocognition and ankle injuries. Table 2 presents a summary of the cognitive tasks used across the 24 studies, organized by the primary neurocognitive domain [48–50]. None of the

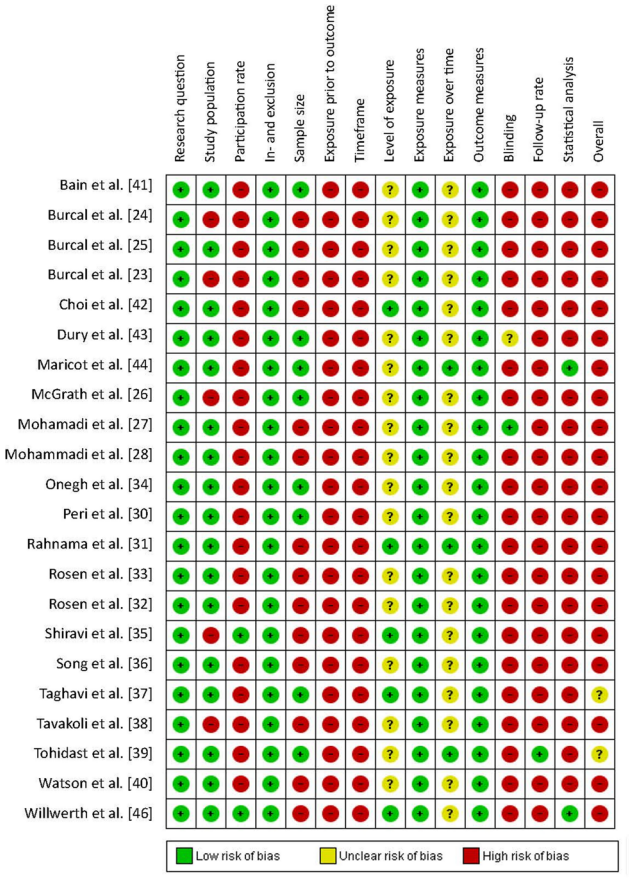

Fig. 2 Study quality assessment for cross-sectional studies within individual studies

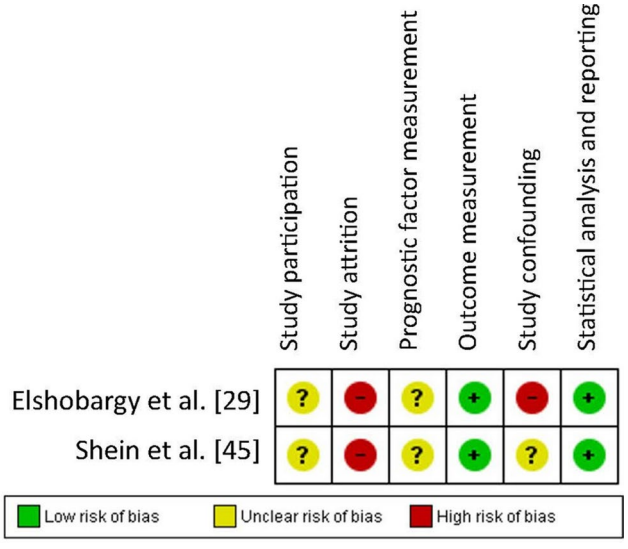

Fig. 3 Study quality assessment for prospective studies within individual studies

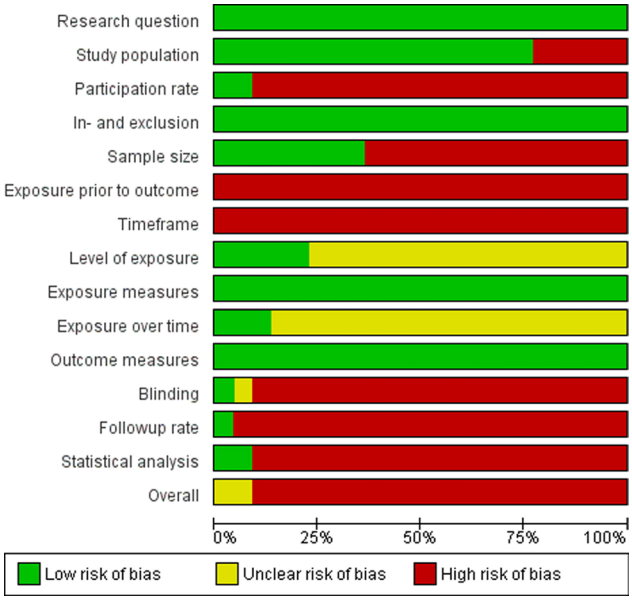

Fig. 4 Study quality assessment for cross-sectional studies across multiple studies

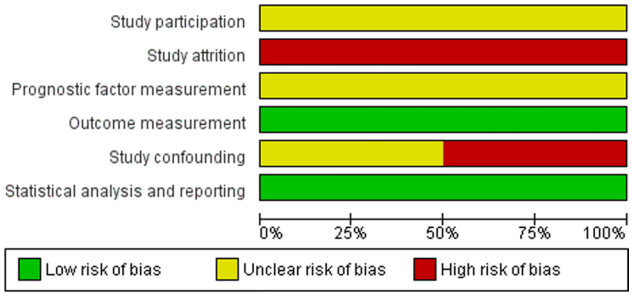

Fig. 5 Study quality assessment for prospective studies across multiple studies

studies investigated whether ligamentous lateral ankle injuries caused changes in neurocognitive function; rather, they examined statistical associations between neurocognitive performance and ankle injury status.

Differences in Neurocognition Between CAI, Copers and Controls

Twenty-four studies focused on differences in neurocognitive performance among individuals with CAI, copers and healthy controls [23–46]. Sixteen investigated dual-task conditions, assessing either cognitive performance during balance or motor tasks, or balance performance under cognitive load. A summary of the findings extracted from the included studies can be found in Table 3.

Attention

Attention was evaluated in four studies, with focus on selective, sustained, and divided attention [32–34, 43]. While two studies found no differences in attention

Table 2 Neurocognitive tasks and domains evaluated across included studies

Cognitive domain	Definition	Cognitive task
Attention	Attention refers to the ability to selectively focus on relevant information while ignoring distractions (selective attention) and maintain this focus over extended periods (sustained attention or vigilance). It also includes the ability to manage multiple streams of information simultaneously (divided attention) [47, 52].	• Attention training [34] • Continuous performance test (CNS Vital Signs) [32, 33] • Shifting attention test [32] • Visual object tracking [43]
Inhibitory control	Inhibitory control or response inhibition refers to the ability to suppress actions or behaviours that are deemed inappropriate, unsafe, or unnecessary [48].	• Go/No-Go Task [30] • Stroop test (auditory and visual variants) [27, 30, 32]
Language skills	Language skills encompass the ability to understand and produce verbal communication. This includes naming, fluency (e.g., generating words within a category), and the ability to follow verbal instructions [47].	• Verbal fluency tasks [46]
Motor skills	Motor skills refer to the execution of physical tasks, including fine motor abilities such as manual dexterity and reaction time, as well as gross motor abilities like balance [47].	• Catch game motor planning test [30] • Finger tapping test [30, 32]
Perception	Perception involves the recognition, interpretation and integration of sensory stimuli, such as identifying objects, sounds, or spatial orientations. It integrates sensory input into meaningful information [47].	• Judgement of line orientation (JLO) [40] • Manikin test [24] • Problem-solving spatial test [30] • Reactive balance test (RBT) [44] • Visual-spatial processing test [30]
Processing speed	Processing speed refers to the ability to quickly complete cognitive tasks, ranging from simple to complex, with an emphasis on performing them as fast as possible [47].	• Choice-reaction hop test [42] • Deary-liewald reaction time task (DLRT) [28] • Staged information processing speed test [30] • Symbol digit modalities (SDM) test [32] • Visuomotor reaction time task [36, 41]
Verbal memory	Verbal memory encompasses the ability to encode, store, and retrieve information presented in verbal form, such as lists of words or narratives [47].	• Verbal memory test (CNS Vital Signs) [32] • Verbal symbol digit Modalities Test [40]
Visual memory	Visual memory refers to the cognitive function that enables the temporary maintenance of visual information relevant for a current or pending task [49].	• Visual memory test (CNS Vital Signs) [32]
Working memory	Working memory is the capacity to hold and manipulate information temporarily for cognitive tasks. It includes maintenance (holding information) and manipulation (reorganizing or processing that information) [47].	• Backward digit span task [31, 45] • Digit counting task (with Audio Recording) [29] • Random number generation (to a metronome) [24, 25] • Serial subtraction task (counting backward by 7 s or 3 s) [23, 24, 26, 31, 35, 37–40] • Summing complex numerical sequences [39]

performance tests between CAI patients, healthy controls [34] and copers [33], Rosen et al. (2021) observed that CAI patients performed worse compared to controls [32].

Dury et al. (2024) reported increased reaction time during a dual-task landing compared to an isolated cognitive test in healthy participants, whereas CAI participants did not exhibit significant changes in reaction time [43]. Cognitive load influenced balance performance in CAI patients and copers with significant correlations observed between attention scores and centre of pressure variables [33]. Increased cognitive demands also led to a longer time to stabilization and greater mediolateral ground reaction forces but no differences between CAI and controls were observed [43]. However, dual-task training improved stability indices in CAI patients, although its benefits did not differ from conventional balance training [34].

Inhibitory Control

Inhibitory control was evaluated in three studies, using the Go/No-Go task and the Stroop test [27, 30, 32], with inhibitory control being impaired in CAI patients compared to copers and healthy controls in one study [32], while another study found no differences between CAI patients and healthy controls [30].

Mohamadi et al. (2020) reported that performing an inhibitory control cognitive task during single-leg balance led to increased reaction time in CAI patients compared to copers and controls, while accuracy did not differ between groups [27]. Rosen et al. (2021) showed increased reliance on attentional resources for postural stability during tasks requiring inhibition [32]. However, it is important to note that these findings may not generalize due to variability in results [27].

Language Skills

One study incorporated a verbal fluency task [46]. The results indicated that a history of ankle sprain injuries did

Table 3 Summary of the findings extracted from the included studies

Author (year)	Study design	In-/exclusion criteria			Participant characteristics			Methods	Outcome Measures	Results
		CAI	*Copers*	*Controls*	*CAI*	*Copers*	*Controls*			
Burcal et al. (2016) [25]	Cross-sectional	Inclusion • History of ≥ 2 LAS; • ≥ 1 episode of giving way < 6 m; • AII: ≥ 4 "yes". Exclusion • Vestibular disorders; Visual disabilities; • Cutaneous sensory dysfunction; • Acute LE injury (other than LAS for the CAI & Coper group) < 6 w; • No head injuries < 6 w; • Chronic MSK conditions known to affect balance; • History of LE surgery.	• History of ≤ 2 LAS + most recent LAS > 12 m; • No giving way < 6 m; • AII: ≤ 3 "yes"; • $FAAM_{ADL}$: > 99%; • $FAAM_S$: > 97%.	• No history of LAS, instability, disability; • AII: No "yes"; • $FAAM_{ADL}$: > 99%; • $FAAM_S$: > 97%.	N = 15 Age: 20.1 (± 2.0) y Height: 169.8 (± 10.6) cm Weight: 65.8 (± 10.6) kg $FAAM_{ADL}$: 100.0 (± 0.0) % $FAAM_S$: 99.8 (± 0.8) % #sprains: 2.3 (± 1.4) #episodes of giving way < 6 m: 3.9 (± 2.0)	N = 15 Age: 20.2 (± 2.1) y Height: 167.1 (± 10.7) cm Weight: 64.1 (± 9.5) kg $FAAM_{ADL}$: 99.4 (± 1.3) % $FAAM_S$: 97.9 (± 3.7) % #sprains: 1.3 (± 0.6)	N = 15 Age: 20.3 (± 4.2) y Height: 165.8 (± 8.3) cm Weight: 70.0 (± 21.5) kg $FAAM_{ADL}$: 88.9 (± 6.7) % $FAAM_S$: 66.0 (± 22.2) %	*Working memory:* RNGT Semmes-Weinstein monofilaments	*Primary*: Accuracy *Secondary*: Light-touch threshold (median index number)	*Primary*: Not reported *Secondary*: CAI & Copers on sinus tarsi: sign. ≠ between baseline and cognitive loading condition, but not in healthy controls • ($\chi 2$ = 9.966, P = .007) CAI Baseline: 4.08 (3.84-4.17) Cognitive load: 4.08 (3.84-4.31) Copers Baseline: 3.84 (3.61-3.84) Cognitive load: 3.84 (3.61-4.08) Controls Baseline: 3.22 (2.83-3.84) Cognitive load: 3.61 (3.61-4.08)
Choi et al. 2024 [42]	Cross-sectional	Inclusion • Physically active (> 90 min of PA/week) • History of ≥ 1 LAS at least 12 m. prior to study participating resulting in inflammatory symptoms • CAIT ≥ 25 • > 1 episodes of giving way in the last 12m Exclusion • History of lower extremity surgeries or fractures • Current signs or symptoms of joint sprain in the lower extremity including pain, swelling, discoloration, or loss of range of motion or strength • Any other health issues or unusual symptoms that could affect the participants' safety or performance.	• Physically active (> 90 min of PA/week) • History of ≥ 1 LAS at least 12 m. prior to study participating resulting in inflammatory symptoms • CAIT ≥ 28 • No episodes of giving way	• CAIT-score ≥ 28 • No history of LAS • no episodes of giving-way	N = 24 Age: 21.87 (± 2.6) y Height: 175.8 (± 8.6) cm Weight: 75.2 (± 13.5) kg CAIT-score: 18.2 ± 5.3	N = 12 Age: 23.2y ± 3.0 Height: 177.4 (± 6.8) vm Weight: 77.7 (± 11.6) kg CAIT-score: 28.4 ± 2.2	N = 15 Age: 23.9 (± 4.3) y Height: 170.3 (± 9.7) cm Weight: 69.2 (± 14.8) kg CAIT-score: 29.5 ± 1.0	Choice-reaction Hop Test	*Primary:* Not reported *Secondary:* Time to perform 10 back to back single-limb hops	*Primary*: Not reported *Secondary*: No significant differences in functional test scores between groups (p > 0.05) Average Choice-reaction Hop Test time: • CAI: 21.8 ± 3.7 • Coper: 20.3 ± 3.0 • Control: 21.9 ± 3.6 Fastest Choice-reaction Hop Test time: • CAI: 20.3 ± 2. 8 • Coper: 18.8 ± 3.1 • Control: 20.3 ± 3.5 For patients with CAI: Correlation between average Choice-reaction Hop Test time and CAIT-score: r = -0.55, p = 0.003 Correlation between fastest Choice-reaction Hop Test time and CAIT-score: r = -0.51, p = 0.006
Mohamadi et al. [27]	Cross-sectional	Inclusion • ≥ 1 LAS < 12m; • 2 ≥ episodes of giving way < 6 m; • $FAAM_{ADL}$ < 90%; • $FAAM_S$ < 80%; • IdFAI > 11; • FAOS < 75% in > 2 categories. Exclusion • History of surgery; • Acute LE musculoskeletal injury > 3 m (other than LAS for the CAI & Coper group); • Vestibular disorders; • Visual disabilities; • Impaired cognitive function.	• ≥ 1 LAS < 12 m; • No giving way; • $FAAM_{ADL}$> 90%; • $FAAM_S$ > 80%; • IdFAI < 11; • FAOS > 75% in > 2 categories.	• No history of LAS; • Physically active adults.	N = 25 Age: 30.8 (± 6.2) y Height: 171.6 (± 8.0) cm Weight: 74.5 (± 10.67) kg BMI: 24.8 (± 3.1) kg/m^2 IdFAI: 20.4 (± 8.5) FAAM: 76.0 (± 24.0) FAOS: 114.3 (± 30.4)	N = 25 Age: 30.3 (± 6.1) y Height: 173.6 (± 10.5) cm Weight: 72.7 (± 10.1) kg BMI: 24.1 (± 1.9) kg/m^2 IdFAI: 6.3 (± 4.2) FAAM: 25.2 (± 10.1) FAOS: 47.3 (± 18.3)	N = 25 Age: 31.0 (± 7.3) y Height: 172.2 (± 10.4) cm Weight: 71.9 (± 9.0) kg BMI: 24.3 (± 2.7) kg/m^2	Auditory Stroop test Force plate + UST in 4 conditions 1) eyes open 2) eyes closed 3) eyes open + auditory stroop 4) eyes closed + auditory stroop	*Primary:* • Accuracy • RT *Secondary* CoP: • Mean sway area (cm²) • Mean range of CoP displacement (cm) • Sway index (cm) • Mean velocity (cm/s)	*Primary:* • Sign. interaction of group + task condition on RT (p = .02) • But not for accuracy (p = .31) RT eyes open: • CAI > copers (p = .001) Mean ≠: 0.17 Cohen's d = 0.81 (0.002-1.63) • CAI > controls (p = .001) Mean ≠: 0.21 Cohen's d = 1.05 [0.22-1.89) RT eyes closed: • CAI > copers (p = .002) Mean ≠: 0.16 Cohen's d = 0.81 (0.14-1.47) • CAI > controls (p = .002) Mean ≠: 0.22 Cohen's d = 1.04 [0.20-1.87) Accuracy not sign. ≠ between groups in all testing conditions. *Secondary:* CAI > Copers & controls for all CoP parameters: Area (p < .001), range (p = .02), sway index (p < .001) & velocity (p < .001)
Author (year)	**Study design**	**In-/exclusion criteria**			**Participant characteristics**			**Methods**	**Outcome measures**	**Results**
		CAI	*Copers*	*Controls*	*CAI*	*Copers*	*Controls*			
Rosen et al. (2017) [33]	Cross-sectional	Inclusion • History of moderate - severe LAS + inflammatory symptoms; • Disruption of PA; • ≥ 2 episodes of giving way ≤ 12 m; • CAIT ≤ 24. Exclusion • History of LE surgery or fracture;	• History of moderate - severe LAS + inflammatory symptoms; • Disruption of PA; • ≤ 1 episode of giving way ≤ 12 m; • CAIT ≥ 28.	• No history of LAS; • No giving way; • CAIT ≥ 28.	N = 15 (M:6, F:9) Age: 22.7 (± 3.4) y Height: 169.8 (± 8.2) cm Weight: 70.2 (± 15.4) kg CAIT: 17.5 (± 5.7)	N = 15 (M:6, F:9) Age: 22.1 (± 2.3) y Height: 172.5 (± 10.4) cm Weight: 71.1 (± 10.4) kg CAIT: 28.4 (± 1.1) #sprains: 1.5 (± 0.8)	N = 15 (M:6, F:9) Age: 22.7 (± 2.3) y Height: 171.3 (± 10.3) cm Weight: 74.9 (± 12.6) kg CAIT:	*Simple attention:* CNS Vital Signs - Continuous Performance Test Force plate	*Primary:* Accuracy *Secondary:* CoP: • Max. range (mm) • Sway index (mm) • Mean velocity (mm/s)	*Primary:* No sign. ≠ between groups. *Secondary:* No sign. ≠ between groups, but sign. small correlations • Simple attention x antero-posterior CoP max. range: r = -0.362, p = .007 • Simple attention x antero-posterior CoP mean velocity: r = 0.274, p = .034 CAI: Moderate – large correlations between simple attention x • Antero-posterior CoP max. range: r = -0.593 (p = .01)

Table 3 (continued)

		• Current signs of joint sprain symptoms in LE; • Health issue or unusual symptom affecting the participant's safety or performance; • Pregnancy; • Vestibular disorders; • impaired cognitive function; • Medication that affects cognitive function.	#sprains: 3.7 (± 3.3) Time since initial injury: 45.6 (± 29.6) m	Time since initial injury: 55.5 (± 29.5) m	29.9 (± 0.4) #sprains: 0.0 (± 0.0) Time since initial injury: 0.0 (± 0.0)			• Medio-lateral CoP max. range: r = -0.472 (p = .04) • Antero-posterior CoP velocity: r = 0.483 (p = .03) <u>Copers:</u> Moderate correlation between simple attention x antero-posterior CoP max. range: r = -0.512 (p = .03) <u>Controls:</u> No correlations between simple attention and CoP variables.
Rosen et al. (2021) [32]	Cross-sectional	<u>Inclusion</u> • > 90 min PA/w • History of moderate – severe LAS + inflammatory symptoms + disruption PA; • ≥ 2 episodes of giving way ≤ 12 m; • CAIT ≤ 24. • > 90 min PA/w • History of moderate - severe LAS + inflammatory symptoms + disruption PA; • ≤ 1 episode of giving way ≤ 12 m; • CAIT ≥ 28. • > 90 min PA/w; • No history of LAS; • No giving way; • CAIT ≥ 28. <u>Exclusion</u> • Female; • History of LE surgery or fracture; • Current signs of joint sprain symptoms in LE; • Health issue or unusual symptom affecting the participant's safety or performance; • Pregnancy; • Vestibular disorders; • impaired cognitive function; • Medication that affects cognitive function.	N = 14 Age: 22.1 (± 3.2) y Height: 178.1 (± 6.4) cm Weight: 84.0 (± 12.5) kg CAIT: 16.0 (± 5.8) #sprains: 4.4 (± 3.0) Time since initial injury: 23.8 (± 25.9) m	N = 13 Age: 22.2 (± 2.4) y Height: 179.5 (± 8.5) cm Weight: 81.1 (± 9.8) kg CAIT: 29.0 (± 0.9) #sprains: 1.4 (± 0.5) Time since initial injury: 27.2 (± 29.0) m	N = 14 Age: 22.6 (± 2.4) y Height: 179.1 (± 7.6) cm Weight: 85.1 (± 12.3) kg CAIT: 29.8 (± 0.4) #sprains: 0.0 (± 0.0) Time since initial injury: 0.0 (± 0.0) m	CNS Vital Signs • Verbal Memory Test • Visual Memory Test • Finger Tapping Test • Symbol Digit Coding Test • Stroop Test • Shifting Attention Test • Continuous Performance Test	*Primary:* • Age normalised, standard individual scores per neurocognitive domain. • Composite score	*Primary:* Composite memory: CAI < Controls CAI: 96.7 (± 15.2) [87.9-105.5] Controls: 112.5 (± 14.5) [103.3-121.7] t = 2.748, p = .024, cohen's d = 1.06 Visual memory: CAI < Controls CAI: 101.4 (± 12.0) [94.4-108.3] Controls: 115.0 (± 11.8) [107.5-122.5] t = 2.898, p = .038, cohen's d = 1.13 Simple attention: CAI < Controls CAI: 93.5 (85.0-97.0) [81.9-98.3] Controls: 108.0 (99.0-108.0) [99.3-108.9] Mann-Witney U = 29.0, p = .003, r = 0.61 Visual memory: Copers < Controls Copers: 100.2 (± 11.4) [89.8+110.3] t = 2.669, p = .025, cohen's d = 1.06 Participants categorised as "low average", "low" or "very low": • CAI: 21.4% • Copers: 18.6% • Controls: 8.3%
Shein Lumbroso et al. (2023) [45]	Prospective cohort study	**In-/exclusion criteria** *CAI* | *Copers* <u>Inclusion</u> • aged 18-35y • up to three weeks after LAS, associated with inflammatory symptoms and interruption of desired physical activity for ≥ 1 day; • aged 18-35y • up to three weeks after LAS, associated with inflammatory symptoms and interruption of desired physical activity for ≥ 1 day; • no ankle injury (bilateral) within 1 year	**Participant characteristics** **CAI** N = 21 (f:13, m:8) Age: 23.6 (± 4.0) y Weight: 79.0 (± 18.1) kg Height: 173.4 (± 11.4) cm BMI: 26.3 (± 6.4) kg/m² Weekly physical activity: 3.9 (±3.7) h CAIT-score: 19.7 (± 1.0)	**Copers** N = 12 (f:8, m:4) Age: 23.7 (± 3.1) y Weight: 68.8 (± 13.6) kg Height: 173.0 (± 11.5) cm	Modified Balance error scoring system (with cognitive task on firm tasks: Backward Digits Span Task) Single-leg drop landing (from 40cm) Drop vertical jump (from 40 cm)	*Primary*: Not reported *Secondary:* # of errors on the modified Balance error scoring system Ability to complete	*Primary:* Not reported *Secondary:* Modified Balance error scoring system outcomes: • Sign. Difference between groups on tandem stance on foam (LAS < CON: 2.9 (± 2.1) < 4.7 (± 2.1), p = 0.04, cohen's d = 0.35

Table 3 (continued)

		• no ankle injury (bilateral) within 1 year before study participation • CAIT < 24 or ankle resprain during follow-up • before study participation • CAIT ≥ 24 and no ankle resprain during follow-up Exclusion • other lower extremity injuries within 3m before study participation • history of ankle fractures and/or surgery; • history of neurological disease, • history of vestibular or visual disturbance, • History of any other pathological abnormalities that could affect the participants' motor performance.		BMI: 22.8 (± 2.4) kg/m² Weekly physical activity: 3.9 (±2.5) h CAIT-score: 27.5(± 0.6)		Willingness to perform	• No sign. difference in other Modified Balance error scoring system tasks ($p > 0.05$) No cognitive tasks within 3w from initial LAS were able to predict instability in 6m ($p > 0.05$).
Author (year)	**Study design**	**In-/exclusion criteria** *CAI*	*Controls*	**Participant characteristics** *CAI*	*Controls*	**Methods**	**Outcome measures**	**Results**
Burcal et al. (2016) [24]	Cross-sectional	Inclusion "Inclusion criteria were consistent with the position statement by the International Ankle Consortium" • No history of LAS. Exclusion • No LE injury (other than LAS for the CAI group) or concussion < 3 m; • No LE surgery.		N = 19 Age: 22.1 (± 5.6) y Height: 169.7 (± 7.7) cm Weight: 73.0 (± 17.3) kg AII: 6.3 # of "yes" $FAAM_{ADL}$: 92.2 (± 10.1) % $FAAM_S$: 79.0 (± 19.7) % #sprains: 3.8 (± 2.5) #episodes of giving-way < 6 m: 2.8 (± 2.0)	N = 20 Age: 22.0 (± 2.0) y Height: 175.0 (± 11.2) cm Weight: 71.3 (± 14.9) kg AII: 0.7 # of "yes" $FAAM_{ADL}$: 99.9 (± 0.3) % $FAAM_S$: 99.2 (± 1.7) % #sprains: 3.8 (± 2.5) #episodes of giving-way < 6 m: 2.8 (± 2.0)	BCT MAN RNGT Force plate	*Primary:* Not reported *Secondary:* Time-to-boundry: min., μ, σ • Antero-posterior • Medio-lateral	*Primary:* Not reported: *Secondary:* No main effect of • Group ($p > .050$) • Group x task interaction ($p > .050$)
McGrath et al. (2020) [26]	Cross-sectional	Inclusion • ≥ 90min PA/w; • History of moderate – severe LAS + inflammatory symptoms + disruption PA; • ≥ 2 episodes of giving way < 12 m; • CAIT ≤ 24. • ≥ 90min PA/w; • No history of LAS; • No giving way; • CAIT ≥ 28. Exclusion • History of LE fracture or surgery; • Current signs of LE joint sprain; • Health conditions affecting safety or sing-leg balance performance (incl. pregnancy); • Impaired cognitive function; • Medication that affects balance or stability.		N = 15 (M:6, F:9) Age: 22.7 (± 3.4) y Height: 170 (± 10) cm Weight: 70.2 (± 15.4) kg CAIT: 17.5 (± 5.7) #sprains: 3.7 (± 3.3) Time since most recent LAS: 28.4 (± 29.5) m	N = 15 (M:6, F:9) Age: 22.7 (± 2.3) y Height: 171 (± 010) cm Weight: 74.9 (± 12.6) kg CAIT: 29.9 (± 0.4) #sprains: 0 Time since most recent LAS: 0 m	*Attention:* SBT Force plate	*Primary:* • Accuracy • Time-to-completion *Secondary:* CoP - Sample entropy: • Antero-posterior • Medio-lateral	*Primary:* Accuracy: Main effect of day: $F_{1,27} = 12.75$, $p = .001$, $d = 0.66$ Day 2 > day 1. • Day 1: 1.47 ± 1.52 • Day 2: 0.62 ± 0.83 No sign. interaction ($F_{1,27} = 0.14$, $p = .712$) or main effect for group ($F_{1,27} = 1.50$, $p = .231$). Time-to-completion: Main effect of day: $F_{1,27} = 28.35$, $p = .001$, $d = 1.01$ Day 2 > day 1. • Day 1: 41.9 ± 21.1 • Day 2: 27.8 ± 16.8

Table 3 (continued)

							No sign. interaction ($F_{1,27}$ = 0.04, p = .843) or main effect for group ($F_{1,27}$ = 0.12, p = .735). *Secondary:* Sample entropy – antero-posterior: dual-task < single-task (p = .008, $F_{1,28}$ = 8.23, d = 0.53) • Dual task: 0.52 ± 0.12 [0.48-0.57] • Single task: 0.58 ± 0.11 [0.53-0.62] No main effect for • Group: $F_{1,28}$ = 0.42, p = .520, d = 0.22 • Group x task interaction: $F_{1,28}$ = 1.42, p = .243 ○ Except for Sample entropy medio-lateral: $F_{1,28}$ = 4.18, p = .05 ○ Post-hoc: no sign. ≠ between tasks in both groups: ▪ CAI: t_{14} = -1.28, p = .221, d = 0.42 ▪ Controls: t_{14} = 1.60, p = .133, d = 0.33

Author (year)	Study design	In-/exclusion criteria		Participant characteristics		Methods	Outcome measures	Results
		CAI	*Controls*	*CAI*	*Controls*			
Mohammadi et al. (2020) [28]	Cross-sectional	Inclusion • 20-30 y; • ≥ 2 sign. LAS < 12 m resulting in pain, swelling and LoF; • ≥ 1 episode of giving way; • No recent LE or lower back injury; • No mechanical instability on anterior drawer & talar tilt test; • No ankle injury < 3 m; • CAIT < 24. Exclusion • Medication that affects neurocognition.	Inclusion • 20-30 y; • No history of LAS; • No giving way.	N = 18 (M:18) Age: 23.3 (± 2.35) y Height: 178 (± 10) cm Weight: 68.2 (± 13.2) kg	N = 18 (M:18) Age: 22.9 (±2.6) y Height: 179 (±13) cm Weight: 67.3 (±12.5) kg	*Detection & identification:* Deary-Liewald Reaction Time Task	*Primary:* Simple RT Choice RT Accuracy	*Primary:* Simple RT CAI > Controls: t = -3.751, p = .001 • CAI: 333.02 ± 40.03 • Controls: 295.88 ± 12.73 Choice RT CAI > Controls: t = -5.262, p = .000 • CAI: 506.20 ± 56.31 • Controls: 419.56 ± 41.34 Accuracy CAI < Controls: t = -3.846, p = .001 • CAI: 1.24 ± 1.18 • Controls: 0.13 ± 0.33
Peri et al. (2021) [30]	Cross-sectional	Inclusion • ≥ 1 sign. LAS > 12 m resulting in pain, swelling and LoF ≥ 1 day;	Inclusion • No history of LAS; • No LE MSK injury	N = 15 (M:7, F:8) Age: 21.5 (± 2) y BMI: 22.9 (± 2.4) kg/m^2 PA: IPAQ	N = 15 (M:6, F:9) Age: 20.3 (± 1.2) y BMI: 22.6 (± 1.9) kg/m^2	*Attention, executive function, visual spatial perception, information processing, control of fine motor skills*	*Primary:* Age-standardised ability sore (scaled to IQ-style score: μ = 100, σ = 15)	*Primary:* • No sign. group ≠: F6,51 = 0.3, p = .930 • Sign. effect of exercise: F6,51 = 2.38, p = .042 Both groups ↑ in: ○ Overall cognitive score: p = .003

		• Recent LAS > 3 m; • ≥ 2 episodes of giving way < 6 m; • AII: "yes" to question 1 + ≥ 4 "yes". Exclusion • Condition that affects neurocognition • Medication that affects neurocognition • Health issues that affect balance		Low: 3 (30%) Moderate: 6 (40%) High: 6 (40%) AII: 6.5 (± 1.3) #sprains: Right: 7 Left: 5 Bilateral: 3	PA: IPAQ Low: 9 (60%) Moderate: 2 (13.3%) High: 4 (26.7%)	NeuroTrax • Stroop test • Go/No-Go response inhibition test • Visual-spatial processing test • Problem-solving spatial test • Staged information processing test • Catch Game motor planning test • Finger Tapping test Biodex Stability System Acute exercise: 20 min moderate- high intensity cycling exercise	*Secondary:* Overall stability index • Antero-posterior • Medio-lateral	▪ CAI: PRE: 98.7 ± 4.1 [94.4-101.0] ▪ CAI: POST: 102.9 ± 4.8 [100.2-105.6] ▪ Controls: PRE: 98.0 ± 6.7 [94.3-101.7] ▪ Controls: POST: 103.1 ± 6.9 [99.3-106.9] ○ Visual-spatial perception: p = .033 ▪ CAI: PRE: 102.8 ± 11.4 [96.5-109.1] ▪ CAI: POST: 108.2 ± 9.6 [102.9-113.5] ▪ Controls: PRE: 98.3 ± 13.5 [90.8-105.8] ▪ Controls: POST: 106.1 ± 12.0 [99.5-112.7] ○ Information processing speed: p = .001 ▪ CAI: PRE: 95.6 ± 8.6 [90.8-100.4] ▪ CAI: POST: 102.8 ± 10.5 [97.0-108.6] ▪ Controls: PRE: 91.8 ± 10.7 [85.9-97.7] ▪ Controls: POST: 102.8 ± 10.6 [96.9-108.7] • No sign. effect of exercise for executive function (p = .766), attention (p = .349) & control of fine motor skills (p = .549) • No sign. goup x exercise interaction: $F_{6,51}$ = 0.3, p = .931 *Secondary:* No overall stability index ≠ between groups before exercise: p = .158 • CAI: median = 1.80 • Controls: median = 1.50 No overall stability index ≠ between groups after exercise: p = .053 • CAI: median = 2.10 • Controls: median = 1.70

Author (year)	Study design	In-/exclusion criteria		Participant characteristics		Methods	Outcome measures	Results
		CAI	*Controls*	*CAI*	*Controls*			
		Inclusion		N = 15 (M:5, F:10)		*Dual-tasking:*	*Primary*	*Primary*

Table 3 (continued)

Rahnama et al. (2010) [31]	Cross-sectional	• 18-30 y; • ≥ 2 sign. LAS < 12 m resulting in pain, swelling and LoF; • ≥ 1 episode of giving way; • No mechanical instability on anterior drawer & talar tilt test; • No ankle injury < 3 m; prior to participation. • No history of LAS; • No giving way. Exclusion • Recent pregnancy; • Vestibular or respiratory disorder; • Auditory deficit; • Neurocognitive impairment; • Diabetes; • Recent LE or lower back injuries; • Medication that affects balance.	Age: 21.1 (± 1.6) y Height: 174 (± 104) cm Weight: 70.7 (± 11.7) kg BMI: 23.1 (± 2.5) kg/m^2 PA: 8.5 (± 4.3) y Dominant tested = 12 Non-dominant limb tested = 3 College basketball or volleyball players	N = 15 (M:3, F:12) Age: 21.5 (±2.5) y Height: 173 (±13) cm Weight: 65.1 (±13.5) kg BMI: Not reported PA 5.5 (±4.3) y Dominant tested = 12 Non-dominant limb tested = 3 College basketball or volleyball	Backward digit span task Biodex Stability System	Accuracy *Secondary* • Antero-posterior stability • Medio-lateral stability • Overall stability index	No main effect of • group: p = .43 • postural difficulty: $F_{2,56}$ = p = .27 No sign. interaction of group x postural difficulty $F_{2,56}$ = 0.27, p = .76 *Secondary* No sign. interactions of • group x postural control x cognitive difficulty • postural x cognitive difficulty Sign. interactions of group x postural difficulty x group x cognitive difficulty for • overall stability index ○ CAI < Controls at level 5: p < .01 ○ But not at level 7: p = .17 • medio-lateral stability ○ CAI < Controls m at level 5: p < .01 ○ But not at level 7: p = .18 Dual task: CAI ↓ in postural stability while dual-task vs. Single-task: ○ overall stability index: p < .01 ○ medio-lateral stability: p = .02 But not in controls: ○ overall stability index: p = .82 ○ medio-lateral stability: p = .70
Song et al. (2021) [36]	Case-control	Inclusion • History of LAS • No history of LAS Exclusion • Acute injury ≤ 3 m; • History of LE surgery; • Condition preventing PA.	N = 18 (M:6; F:12) Age: 19.1 (± 1.0) y Height: 170.5 (± 9.6) cm Weight: 64.7 (± 9.5) kg #sprains: 2.4 (± 1.2) Time since most recent LAS: 14.6 (± 8.2) m	N = 33 (M:14; F:19) Age: 18.8 (± 1.0) y Height: 173.1 (± 9.7) cm Weight: 67.9 (± 10.1) kg #sprains: 0.0 (± 0.0)	Upper-extremity Visuomotor RT task	*Primary* • RT • Accuracy	*Primary* RT: CAI > Controls: p = .037, Hedges g = 0.62 [0.03-1.20] • CAI: 0.48 (± 0.04) s • Controls: 0.47 (± 0.04) s Accuracy: No sign. ≠ between groups. #hits: p = .147, Hedges g = -0.43 [-1.01, 0.16] • CAI: 80.39 (± 18.81) • Controls: 87.76 (± 16.07) #misses: p = .229, Hedges g = 0.35 [-0.23-0.93] • CAI: 15.56 (± 9.16) • Controls: 12.96 (± 6.03)
Tohidast et al. (2021) [39]	Cross-sectional	Inclusion • 20-40 y; • History of LAS < 2 y with LoF; • Aged 20-40 y; • ≥ 2 episodes of giving way ≤ 2 y; • BMI = 18-25. Matched according to • Sex; • Age; • BMI. Exclusion	N = 16 Age: 26.1 (± 7.1) y Height: 171.5 (± 9.1) cm Weight: 68.4 (± 12.1) kg	N = 16 Age: 26.2 (± 5.6) years Height: 173.1 (± 7.7) cm Weight: 67.3 (± 10.5) kg $FAAM_S$: 100 (± 0.0)	BCT (easy task) Counting and summing numbers (difficult task) Whole-body vibration	*Primary* Accuracy *Secondary* CoP	*Primary* Not reported *Secondary* No ≠ between groups during BCT (easy task), but sign. ≠ in σ of CoP displacement during difficult task in y-axis when: • eyes open: p = .01, mean difference = -2.1

		• Prior exposure to whole-body vibration or contraindications for therapeutic use; • No LE surgery, fracture or motor deficit; • Balance disorder; • Foot paresthesia.		$FAAM_{ADL}$: 100 (± 0.0) PA: 7.1 (±3.9) h/w			○ CAI > Controls: σ = 1.3 (1.7) > σ = 1.1 (2.6) • eyes closed: p = .003, mean difference = 10.06 ○ CAI > Controls: σ = 2.4 (9.1) > σ = 1.4 (2.9) Sign. ≠ in μ of x-axis displacement between groups in eyes-closed condition: p = .04 ○ CAI > Controls: μ = 1.6 (37.6) > μ = 1.1 (23.0)

Author (year)	**Study design**	**In-/exclusion criteria**		**Participant characteristics**		**Methods**	**Outcome measures**	**Results**
		CAI	*Controls*	*CAI*	*Controls*			
Tavakoli et al. (2016) [38]	Cross-sectional	Inclusion • ≥ 1 moderate-severe LAS > 12 m resulting in pain, swelling, limited weight bearing or full immobilisation > 2 d • Failure to return to preinjury function • ≥ 2 episodes of giving way ≤ 12 m; • 3x/w PA; • Anterior drawer test and talar tilt test score = 2 or 3; • $FAAM_{ADL}$ ≤ 90%; • $FAAM_S$ ≤ 80%.	• Age-matched to CAI patients; • No history of LAS; • 3x/w PA; • $FAAM_{ADL}$ = 100; • $FAAM_S$ = 100; • No foot or ankle disorder or surgery.	N = 21 (M:11, F:10) Age: 25.6 (± 4.8) y Height: 172 (± 12) cm Weight: 67.3 (± 15.3) kg $FAAM_S$: 63.4 (± 16.9) $FAAM_{ADL}$: 80.9 (± 7.7) PA: 9.2 (± 5.5) h/w #Giving way episodes and sprains: 6.4 (± 3.7) (n/y)	N = 19 (M:11, F:8) Age: 25.0 (± 3.1) y Height: 174 (± 9) cm Weight: 67.0 (± 13.6) kg $FAAM_S$: 100 (± 0.0) $FAAM_{ADL}$: 100 (± 0.0) PA: 7.1 (± 3.9) h/w	BCT 3D motion capture system.	*Primary* • Accuracy *Secondary* Foot and leg kinematics during: • Normal walking • Walking + cognitive task • Sitting + cognitive task	*Primary* Sitting condition: • No sign. ≠ in both outcomes between groups: p > .05 • CAI: 15.95 ± 4.45 • Controls: 18.50 ± 4.16 Dual task walking: Accuracy: CAI < Controls: p = .04, ES = 0.69 • CAI: 12.16 ± 3.35 • Controls: 14.89 ± 4.4 Sitting vs. Dual-task walking: p < .001 CAI: ES = 1.01 Controls: ES = 1.15 *Secondary* Both groups walked slower under dual-task conditions with no sign. ≠ in stride velocity (p > .05) Controls: No sign. ≠ in kinematic data between single and dual task walking: p > .05 CAI: • ↑ inversion during dual task walking vs. single task walking at initial contact: p = .03, ES = 0.78 • ↑ plantar flexion during dual task walking vs. single task walking at ○ 100ms pre initial contact: p = .01, ES = 0.71 ○ 200ms post initial contact: p = .03, ES = 0.53 CAI > Control during dual task walking: Plantar flexion

Table 3 (continued)

		Exclusion • vestibular, visual, auditory, cognitive, metabolic, musculoskeletal or other disorders; • History of fracture or surgery; • Medication that affects cognition or performance; • Ankle rehab; • Acute clinical signs & symptoms in LE; • Ankle sprain ≤ 3m.					• 200ms pre initial contact: p = .01, ES = 0.67 Inversion • 200ms pre initial contact: p = .00, ES = 0.96 • 100ms pre initial contact: p = .03, ES = 1.3 • at initial contact: p = .00, ES = 0.97 • 100ms post initial contact: p = .02, ES = 0.83 • 200ms post initial contact: p = .02, ES = 0.81
Author (year)	**Study design**	**In-/exclusion criteria** *CAI* / *Controls*	**Participant characteristics** *CAI*	*Controls*	**Methods**	**Outcome measures**	**Results**
Watson et al. (2020) [40]	Cross-sectional	Inclusion • ≥ 1 LAS > 12 m; • IdFAI score ≥ 11. / • No history of LAS; • No history of LE injuries; • IdFAI ≤ 10. Exclusion • No LE injury ≤ 3m; • Vestibular or cognitive deficits.	N = 16 (M:7; F:9) Age: 21.4 (± 2.2) y Height: 174.2 (± 8.5) cm Weight: 73.7 (± 12.9) kg IdFAI: 16.4 (± 4.0)	N = 17 (M:9; F:8) Age: 21.7 (± 3.1) y Height: 171.8 (± 9.8) cm Weight: 69.7 (± 14.4) kg IdFAI: 1.6 (± 2.7)	*Visuospatial ability* Benton's judgement of line orientation *Verbal memory* Symbol digit modalities test *Quantitative ability* Serial seven substraction Muscle activation	*Primary:* Accuracy Time-to-completion *Secondary:* Antero-posterior stability Medio-lateral stability Vertical stability index Dynamic postural control index	*Primary* Symbol digit modalities test accuracy: CAI > Controls: p = .020 [-3.85;-0.36] 99.01 (± 1.90) > 96.90 (± 2.91) *Secondary* Dynamic postural stability index: No sign. ≠ between groups in any direction or task combination. Muscle activation: • Tibialis anterior muscle: ○ No sign. ≠ 3-way interaction in mean activation: F = 0.350, p = .909, η^2 = 0.011. ○ Task x group effect: F = 3.312, p = .023, η^2 = 0.097, but pairwise comparisons revealed no sign. ≠ between groups. • Peroneus longus muscle: ○ No sign. ≠ 3-way interaction in mean activation $F_{6,186}$ = 1.238, p = .289, η^2 = 0.041 ○ No sign. task x group effect: F = 1.315, p = .274, η^2 = 0.041 • Gastrocnemius lateralis muscle: ○ No sign. ≠ 3-way interaction in mean activation $F_{6,186}$ = 1.660, p = .133 η^2 = 0.051 ○ No sign. task x group interaction: F = 1.406, p = .246, η^2 = 0.043
Willwerth et al. 2023 [46]	Cross-sectional study	*LAS* / *Controls* Inclusion • Division-I varsity athletes • History of ≥ 1 ankle sprain / • Division-I varsity athletes • No history of ankle sprains Exclusion	*LAS* N = 29 (M:15, F:14) Age : 19.7 (±0.9) y Height : 179.8 (±11.1) cm Weight : 80.1 (±20.7) kg BMI : 25.5 (±4.7) kg/m^2	*Controls* N = 31 (M:18, F:13) Age : 19.3 (±0.8) y Height : 178.2 (±11.7) cm	*Gait assessment* Gait Analyzer app	*Primary* Cognitive performance: • response rate • response time • response accuracy	*Primary* No significant difference in cognitive performance between groups (p = 0.35): • response rate (words per minute), Cohen's d = −0.02

		• History of lower extremity surgeries or current injuries • History of concussion • Missing or incomplete intake forms	Ankle sprain history: • 1 sprain: 18 athletes, 27 limbs • 2 sprains: 7 athletes, 13 limbs • 3 sprains: 3 athletes, 3 limbs • 5 sprains: 1 athlete, 1 limb Time since injury = 24 months	Weight : 79.9 (±21.5) kg BMI : 24.9 (±4.2) kg/m^2		*Secondary* Spatiotemporal gait parameters • step time • step length • gait velocity • cadence • step symmetry • total distance • vertical displacement	• average response time (ms), Cohen's d = −0.17 • accuracy (%),Cohen's d = 0.23 *Secondary* No significant differences between groups for any gait parameters (p = 0.75) • step time (s), Cohen's d = 0.10 • step length (m), Cohen's d = 0.06 • gait velocity (m/s), Cohen's d = 0.16 • cadence (steps/min), Cohen's d = −0.03 • step symmetry (%), Cohen's d = 0.06 • total distance (m), Cohen's d = 0.35 • vertical displacement (cm), Cohen's d = 0.19
		CAI / *Controls*	*CAI*	*Controls*			
Maricot et al. (2024) [44]	Retrospective case-control	Inclusion • Age = 18-35 • At least active in 1 sport/workout • history of at least one LAS at least 12 months prior to study enrolment associated with inflammatory symptoms • the initial sprain created at least one interrupted day of desired physical activity • the most recent injury more than three months before study enrolment, • recurrent sprains or "feelings of giving way" • at least two episodes of giving way six months before study enrolment • CAIT score <24 / • Age = 18-35 • At least active in 1 sport/workout • not meet the CAI inclusion criteria Exclusion	N = 27 Age : 22 (±2.3) y Height : 175.8 (±10.3) cm Leg length : 84.7 (±6.0) cm Weight: 71.4 (±10.1) kg IPAQ : 4560 (±2322) MET/week	N = 21 Age : 23 (±1.1) y Height : 172.0 (±10.0) cm Leg length : 87.3 (±5.7) cm Weight : 68.5 (±8.5) kg IPAQ : 2963 (±2246.1) MET/week	Y-balance test RBT	*Primary:* Accuracy *Secondary:* VMRT	*Primary* • no main effect of group for accuracy (p = 0.324) • Interaction of physical activity with YBT-score for accuracy (p = 0.013, F = 3.911, partial η2 = 0.157). • differences between CAI patients with affected side and healthy controls (p = 0.015) with a mean differences of 8.7 (±3.0)% in favour of controls *Secondary* • No main effect of group (p = 0.327) and no interaction for VMRT (p < 0.423)

Table 3 (continued)

		• history of a lower-limb fracture • previous (< 2 years) surgery to musculoskeletal structures (i.e., bones, joint structures, nerves) in either lower limb any other relevant medical history, treatment or current condition (such as neurological diseases, inner ear disorders, color blindness)					
Author (year)	**Study design**	**In-/exclusion criteria** CAI	**Participant characteristics** CAI		**Methods**	**Outcome measures**	**Results**
Burcal et al. (2016) [23]	Cross-sectional	Inclusion • History of ≥ 2 LAS; • ≥ 1 episode of giving way < 3 m; • AII : ≥ 4 "yes". Exclusion • No head injuries < 6w.	N = 24 (M:7, F:17) Age: 21.3 (± 2.0) y Height: 169.8 (± 12.9) cm Weight: 72.5 (± 22.2) kg $FAAM_{ADL}$: 85,3 (± 7.9) % $FAAM_{S}$: 68,6 (± 12.9) % AII:6.29 (± 1.52) #sprains: 3.88 (± 2.53) #episodes of giving way: 3.37 (± 2.28)		BCT Force plate	*Primary* Not reported *Secondary* CoP • Antero-posterior σ & velocity • Medio-lateral σ & velocity	*Primary* Not reported *Secondary* #episodes of giving way x antero-posterior velocity: r = .567 #episodes of giving way x medio-lateral velocity: r = 0.562 Antero-posterior σ = 0.99 (± 0.39) Antero-posterior velocity 0.93 (± 0.28) Medio-lateral σ = 1.00 (± 0.24) Medio-lateral velocity 1.05 (± 0.21)
Elshorbagy et al. (2022) [29]	Prospective	Inclusion • 18-35y; • ≥ 1 acute resulting in pain, swelling, LoF; • No LAS < 3 m; • > 1 episode of giving way < 6m. Exclusion • MSK dysfunction; • Fracture; • LE disease other than LAS to the LE; • Deformities of the LE; • Posture malalignement; • Pathological disease that affects coordination: vestibular disorders, middle ear; • Any neurological condition; • Any condition that affects cognitive function or focus of attention; • Training with the Biodex Balance System; • BMI > 25 or < 18.	Group A N = 14 Age: 22.9 (± 4.3) y Height: 161.9 (± 9.2) cm Weight: 64.1 (± 13.1) kg Group B N = 15 Age: 24.1 (± 5.2) y Height: 162.7 (± 9.2) cm Weight: 70.4 (± 8.4) kg Group C N = 14 Age: 35.9 (± 3.7) y Height: 165.4 (± 3.9) cm Weight: 74.7 (± 4.0) kg		External focus of attention Internal focus of attention Continuous cognitive task (counting task) Biodex Balance System	*Primary* Not reported *Secondary* • Antero-posterior stability • Medio-lateral stability • Overall stability index	*Primary* Not reported *Secondary* No sign. ≠ within groups in all stability indexes at both task difficulties. Continuous cognitive task > external focus for all stability indexes: • antero-posterior stability: ○ Level 5: p = .006, 5.28 ± 2.75 > 2.99 ± 1.01 ○ Level 7: p = .015, 4.52 ± 2.53 > 2.59 ± 0.81 • medio-lateral stability: ○ Level 5: p = .000, 4.76 ± 2.21 > 2.07 ± 0.59 ○ Level 7: p = .000, 3.94 ± 1.57 > 1.99 ± 0.70 • overall stability index: ○ Level 5: p = .000, 7.52 ± 3.14 > 3.31 ± 0.92 ○ Level 7: p = .000, 6.24 ± 2.73 > 3.21 ± 1.08 Continuous cognitive task > internal focus for the overall and medio-lateral stability indexes: • antero-posterior stability: ○ Level 5: p = .183, 5.28 ± 2.75 > 3.75 ± 0.90 ○ Level 7: p = .204, 4.52 ± 2.53 > 3.66 ± 2.47

Table 3 (continued)

						• medio-lateral stability: ○ Level 5: p = .019, 4.76 ± 2.21 > 4.67 ± 2.21 ○ Level 7: p = .001, 3.94 ± 1.57 > 3.92 ± 1.57 • overall stability index: ○ Level 5: p = .006, 7.52 ± 3.14 > 4.59 ± 1.00 ○ Level 7: p = .018, 6.24 ± 2.73 > 4.15 ± 2.29
Onegh et al. (2020) [34]	Cross-sectional	Inclusion • 18-52 y; • Unilateral instability; • ≥ 1 LAS < 12 m; • ≥ 1 episode of giving way (frequent); • No mechanical instability on anterior drawer & talar tilt test; • No history of vertigo/fainting; • No ankle pain/inflammation; • No visual/auditory/verbal/MSK/LE/back disorder. Exclusion • Symptoms during the treatment; • Receiving other treatment; • Failure to progress in early stages of attention training.	Biodex Balance Training N = 15 (M:8, F:7) Age: 9.9 (± 31.1) y Height: 89 (± 164) cm Weight:19.4 (± 71.8) kg BMI: 5.8 (± 26.4) kg/m^2 Dual-task training N = 17 (M:5, F:12) Age: 34.8 (± 11.2) y Height: 89 (± 163) cm Weight: 15.8 (± 70.4) kg BMI: 5.5 (± 26.4) kg/m^2	Intervention: attention training Biodex Balance System	*Primary* Not reported *Secondary* • Antero-posterior stability • Medio-lateral stability • Overall stability index	*Primary:* Not reported *Secondary:* Dual task training: p > .05 on all stability indexes for all difficulty levels on single and both leg stance and eyes open and closed: • Antero-posterior stability: p = [.000 - .026] • Medio-lateral stability p = [.000 - .008] • Overall stability index p = [.000 - .005] Dual task training not sign. ≠ balance training for all variables: p > 0.05: • Antero-posterior stability: p = [.26 – 0.70] • Medio-lateral stability p = [.17 - .86] • Overall stability index p = [.30 – 0.84]
Bain et al. (2023) [41]	Cross-sectional	Inclusion • Female • Age: 18-35 • History of LAS & • Sustained LAS > 6 months Exclusion • History of lower-extremity fracture/surgery/balance/vestibular disorders	N = 24 Age = 24 (± 3) Height = 163.9 cm (± 9.8) Mass = 65.5 kg (± 11.5) $N_{LAS\ left}$ = 16, $N_{LAS\ right}$ = 4 Grade of initial LAS: N_{gr1} = 5; N_{gr2} = 14, N_{gr3} = 3	Questionnaires: • FADI • mDPA • FABQ • TSK-11 • PSWQ Single-limb balance: the FITLIGHT Trainer • VMRT	*Primary* Not reported *Secondary* Association between scores on questionnaires and VMRT of injured and uninjured limb	*Primary:* Not reported *Secondary:* Strong negative correlation between: • FADI-ADL & injured limb VMRT (r = -0.65, p = 0.001) • FADI-sport & injured limb VMRT (r = -0.66, p = 0.001) • FADI total scores and injured limb VMRT (r = -0.70, p < 0.001) moderate, negative correlation between: • FADI-ADL & uninjured limb VMRT (r = -0.54, p = 0.01) • FADI-Sport & uninjured limb VMRT (r = -0.54, p = 0.01) • FADI-Total scores & uninjured limb VMRT ((r = -0.54, p = 0.01) Moderate positive correlation between: • PA-PSC & uninjured limb VMRT (r = 0.53, p = 0.01)),

Table 3 (continued)

						• mDPA-Total scores & uninjured limb VMRT (r = 0.43, p = 0.04)
Author (year)	**Study design**	**In-/exclusion criteria** *CAI*	**Participant characteristics** *CAI*	**Methods**	**Outcome measures**	**Results**
Shiravi et al. (2017) [35]	Cross-sectional	Inclusion • 18-36 y; • History of non-acute, non-operated ankle sprain; • ≥ 1 LAS; • ≥ 1 episode of giving way ≤ 6 m. Exclusion • History of visual, vestibular or neurological disorder; • Auditory or cognitive deficit (memory); • Diabetes; • Medication that affects balance.	N = 8	Digit-backward counting Force plate	*Primary* Not reported *Secondary* CoP • Area • μ sway • μ velocity	*Primary* Not reported *Secondary* • Cognitive task had no sign. effect on CoP variables with either eyes close or open: p > 0.05. • No difference in medio-lateral sway during dual-task between the injured (p = 0.24) and non-injured leg (p = 1.000) • After cognitive task → CoP area ↓ in both limbs: p = .04 • No sign. ≠ in all CoP variables between limbs.
Taghavi et al. (2022) [37]	Cross-sectional	Inclusion • 18-25 y; • Active men; • BMI = [18-25]; • ≥ 1 moderate-severe LAS resulting in pain, LoF > 1 d; • ≥ 2 episodes of giving way > 6 w; • Ability to weight bear on injured limb; • FADI < 90%; • FADI-S < 80%. Exclusion • History of vestibular or neuro-MSK disorders; • LE Surgery; • LE injury ≤ 6m; • Medication that affects balance; • MSK abnormalities in LE; • Physiotherapy ≤ 3 m.	Wobble board training with cognitive intervention N = 7 (M:7) Age: 22.4 (± 2.2) y Height: 177.6 (± 5.8) cm Weight: 72.7 (±3.8) kg BMI: 21.6 (± 1.0) kg/m^2 Wobble board training N = 7 (M:7) : Age: 23.1 (± 1.3) y Height: 174.4 (± 6.4) cm Weight: 74.6 (± 6.4) kg BMI:22.3 (± 0.7) kg/m^2 Control patient group N = 7 (M:7) Age 22.4 (± 2.4) y Height: 176.6 (± 5.9) cm Weight: 76.4 (± 3.5) kg BMI: 22.3 (± 0.7) kg/m^2	Digit-backward counting Biodex 2 isokinetic dynamometer Single-leg jump landing task Y-Balance Test Balance Error Scoring System	*Primary* Not reported *Secondary* • Proprioception • Jump landing kinetic variables • Dynamic & static balance	*Primary* Not reported *Secondary* Both groups improved compared to controls for all proprioceptive tasks + sign. main group effect: • Active 15°: $F_{2,28}$ = 25.72, p = .001, η^2 = 0.75 ○ Training with cognitive intervention: t = -6.74, p = .001 ○ Training: t = -6.53, p = .001 • Passive 15°: $F_{2,28}$ = 33.66, p = .001, η^2 = 0.79 ○ Training with cognitive intervention: t = -6.94, p = .001 ○ Training: t = -5.90, p = .001 • Active max. Inversion: $F_{2,28}$ = 20.47, p = .001, η^2 = 0.70 ○ Training with cognitive intervention t = -14.94, p= .001 ○ Training: t = -5.64, p = .001 • Passive max. Inversion: $F_{2,28}$ = 9.16, p = .002, η^2 = 0.51 ○ Training with cognitive intervention: t = -5.38, p = .002 ○ Training: t = -6.47, p = .001 Control patients did not show any changes over time: p > 0.05. Both intervention groups did not sign. ≠ from each other: p > .05 Both groups improved compared to controls for all jump landing kinetic variables + sign. main group effect: • Mediolateral CoP (cm): $F_{2,18}$ = 31.33, p = .001, η^2 = 0.78 ○ Training with cognitive intervention: t = -6.15, p = .001

Table 3 (continued)

						○ Training: t = -6.42, p = .001 • Mediolateral time to stabilisation (s): $F_{2,18}$ = 19.48, p = .001, η^2 = 0.69 ○ Training with cognitive intervention: t = -3.66, p = .010 ○ Training: t = -6.49, p = .001 • Anteroposterior CoP (cm): $F_{2,18}$ = 30.72, p = .001, η^2 = 0.78 ○ Training with cognitive intervention: t = -5.40, p = .002 ○ Training: t = -6.33, p = .001 • Anteroposterior time to stabilisation (s): $F_{2,18}$ = 16.46, p = .001, η^2 = 0.66 ○ Training with cognitive intervention: t = -3.42, p = .014 ○ Training: t = -4.96, p = .001 • Resultant vector time to stabilisation (s): $F_{2,18}$ = 52.16, p = .001, η^2 = 0.86 ○ Training with cognitive intervention: t = -5.43, p = .002 ○ Training: t = -6.83, p = .001 Control patients did not show any changes over time: p > 0.05. Both intervention groups did not sign. ≠ from each other: p > .05 Both groups improved compared to controls for all static & dynamic balance variables + sign. main group effect: • Dynamic balance: $F_{2,18}$ = 6.09, p = .010, η^2 = 0.41 ○ Training with cognitive intervention: t = 2.53, p = .045 ○ Training: t = -2.82, p = .030 • Static balance: $F_{2,18}$ = 54.68, p = .001, η^2 = 0.86 ○ Training with cognitive intervention: t = -7.89, p = .001 ○ Training: t = -6.95, p = .001 Control patients did not show any changes over time: p > 0.05. Both intervention groups did not sign. ≠ from each other: p > .05

Legenda

BCT = Backward Counting test: BMI = Body Mass Index; CAI = chronic ankle instability; CAIT = Cumberland Ankle Instability Tool; CNS = Computerized Neurocognitive Screening; CoP = center of pressure; d = day(s); DT = dual task; DTPOS = dual task after fatigue; DTPRE = dual task before fatigue; F = female; $FAAM_{ADL}$ = Foot and Ankle Ability Measure Activities of Daily Living; $FAAM_S$ = Foot and Ankle Ability Measure Sport; FABQ = Fear-Avoidance Beliefs Questionnaire ; FADI = Foot and Ankle Disability index; FADI-S = Foot and Ankle Disability index sport; FAOS = Foot and Ankle Outcome Score; GRF = ground reaction force; h = hour(s); h/w = hour(s) per week; IdFAI = identification of Functional Ankle Instability; Incl. = including; IPAQ = International Physical Activity Questionnaire; LAS = lateral ankle sprain; LE = lower extremity; LoF = loss of function; M = male; m = month(s); MAN = Manikin test; Max. = maximal; MET = metabolic equivalent of task; mDPA = modified Dis- oriented physically Active Scale; min = minute(s); MSK = musculoskeletal; n/y = time(s)per year; PA = physical activity; PSWQ = Penn State Worry Questionnaire; RBT = Reactive balance test; RNGT = Random Number Generation test; ROM = range of motion; RT = reaction time; SBT = Serial Subtraction task; Sign. = significant; ST = single task; STPOS = single task after fatigue; STPRE = single task before fatigue; TSK-11 = Tampa Scale of Kinesiophobia; UST = Unilateral Stance Test; VMRT = Visual motor reaction time; w = week(s); x = and; y = year(s); ≠ = difference; # = total; μ = mean; σ = standard deviation

not significantly impact verbal fluency. Also, a history of ankle sprain injuries did not significantly impact spatio-temporal gait outcomes during the clinical assessment [46].

Motor Skills

Two studies [30, 32] focused on the assessment of motor skills related to LAS and CAI. No differences were found between CAI and healthy controls on the Catch Game Motor Planning Test and the Finger Tapping Test [30, 32].

Perception

Four studies focussed on perception in their research [24, 30, 40, 44]. Perceptual abilities, including visual-spatial processing, did not differ between CAI patients and healthy controls [30, 40].

Individuals with CAI demonstrated lower accuracy on the Reactive Balance Test compared to controls, although visuomotor reaction times remained comparable between groups and across injured and non-injured legs [44]. While healthy participants exhibited reduced dynamic postural stability under cognitive load compared to balance without cognitive load, individuals with CAI showed no significant changes in balance performance across conditions [40]. Similarly, Burcal et al. (2016) reported no significantly altered balance measures in either individuals with CAI or controls with addition of a perception task [24].

Processing Speed

Six studies investigated processing speed [28, 30, 32, 36, 41, 42]. No significant differences were observed between CAI patients and healthy controls on tests such as the Staged Information Processing Speed Test [30] or Symbol Digit Coding [32]. However, CAI patients demonstrated slower reaction times and increased errors on the Deary-Liewald Reaction Time Task compared to controls [28]. Similarly, patients with a history of ankle sprain exhibited longer reaction times on visuomotor tasks [36] with slower reaction times associated with poorer health-related quality of life scores and the injured limb exhibiting stronger associations with health-related quality of life outcomes than the uninjured limb [41].

Neurocognitive hop performance on the Choice-Reaction Hop Test was comparable across CAI, coper, and control groups, although reaction times on the Choice-Reaction Hop Test negatively correlated with ankle instability severity in CAI patients [42].

Verbal Memory

Two studies included verbal memory [32, 40]. Individuals with CAI showed significant deficits in visual memory compared to controls, with large effect sizes [32, 40]. Also, copers showed reduced visual memory compared to controls [32]. Balance performance remained unaffected in CAI patients with addition of a verbal memory task [40].

Visual Memory

One study investigated visual memory [32]. Deficits in visual memory scores were reported in individuals with CAI compared to controls. Additionally, copers also exhibited deficits in visual memory compared to controls [32].

Working Memory

Twelve studies included working memory [23–26, 29, 31, 35, 37–40, 45]. No significant differences were found in cognitive performance related to working memory between individuals with CAI and healthy controls [26, 31, 38–40].

When cognitive tasks were paired with postural challenges, faster completion time and fewer errors were observed compared to performance on the isolated cognitive task [26]. No significant differences in cognitive performance were observed between CAI patients and controls during these dual-task scenarios [31]. When paired with walking, cognitive performance on executive function tasks worsened across groups, with CAI patients enumerating fewer correct answers compared to controls [38]. Working memory tasks influenced balance performance differently across studies. While some findings suggested that addition of a cognitive task stabilizes balance by reducing postural sway in CAI patients [35] and healthy controls [24], others reported increased sway in CAI patients [29] compared to controls [23, 31] or compared to copers and controls [27]. Watson et al. (2020) found that healthy participants demonstrated worse dynamic postural stability under Serial Sevens cognitive load compared to balance without cognitive load, but this effect was not observed in CAI patients [40]. However, few studies reported no differences in balance with or without cognitive load in patients with CAI [37]. Lumbroso et al. (2023) observed significant differences during the foam tandem stance task while performing the Backward Digit Span Task, where potential copers scored lower than non-copers [45]. Finally some studies found equally impaired stability with addition of a working memory task in both CAI patients and healthy controls [26, 39], with Tohidast et al. (2021) reporting no difference between CAI patients and healthy controls during single leg stance while performing backward counting by 3 s (easy task), but worse balance performance in CAI patients compared to controls during summing complex numerical sequences (difficult task) [39]. Overall, cognitive tasks were found to reduce postural sway during single-leg stance, with no significant differences observed between CAI and controls [24].

No additional benefit was found in incorporating cognitive intervention into Wobble Board Training for improving proprioception or jump-landing kinetic variables in individuals with CAI [37]. In both CAI patients and healthy controls, peroneus longus activation was lowest during the Serial Sevens cognitive load task compared to visuospatial perception and processing speed tasks [40]. Furthermore, the backward digit span task within three weeks of a lateral ankle sprain did not predict instability at six months [45]. Dual-task walking conditions led to slower walking speeds in both CAI patients and healthy controls, with no group differences in stride velocity. However, CAI patients exhibited increased ankle inversion and plantarflexion during dual-task walking compared to single-task conditions, while no such kinematic changes were observed in controls [38]. Additionally, dual-task conditions raised plantar cutaneous sensation thresholds in CAI patients, copers, and controls [25].

Discussion

This systematic review synthesized evidence on the relationship between neurocognitive performance and ligamentous ankle injuries, with most studies focusing on CAI.

In the context of CAI, several neurocognitive domains have been investigated, highlighting the complex interaction between cognitive processing and motor control. The findings indicate that CAI patients exhibit deficits in selective and divided attention, inhibitory control, and visual memory, with mixed results for working memory and processing speed. Notably, some domains, such as language and motor skills, showed no significant deficits. These results suggest that CAI may influence certain neurocognitive performance elements, likely due to altered sensorimotor integration and compensatory strategies. However, inconsistencies across studies and the absence of significant differences in several areas warrant cautious interpretation.

These results align with existing literature on the role of neurocognition in injury mechanisms, including ACL injuries and musculoskeletal injuries more broadly. Research on ACL injuries by Bertozzi et al. (2023) highlights that lower cognitive performance in domains such as reaction time, working memory, and visual-spatial processing is associated with biomechanical patterns increasing injury risk, such as increased knee valgus angles and anterior tibial shear forces, particularly during dual-task or unanticipated movements [51]. Swanik et al.

(2007) indicate that differences in neurocognitive performance may contribute to diminished neuromuscular control and coordination errors, increasing the susceptibility of certain intercollegiate athletes to noncontact ACL injuries [21]. More generally, Wilke et al. (2022) demonstrated that slower reaction times and impaired visuomotor processing predict higher musculoskeletal injury risk in open-skill sports like soccer and basketball, where rapid cognitive processing and adaptation are essential [52].

Neurocognitive deficits in CAI patients during tasks requiring divided attention or inhibitory control are particularly evident under dual-task conditions where cognitive load influences motor and balance performance. Dual-tasking not only challenges the cognitive domains targeted by the cognitive task but also heavily taxes attention, specifically divided attention, as it requires allocating focus between the physical and cognitive tasks [53]. Deficits in selective and divided attention are demonstrated in individuals with CAI [32–34, 43]. These challenges can be explained by several dual-task theories. The capacity-sharing theory posits that attentional resources are limited, leading to a decline in performance of one or both tasks when they demand substantial attention [54]. Similarly, the bottleneck theory suggests that tasks requiring the same neural processors create a bottleneck, delaying the second task until the processor is free [54]. In contrast, multiple resource models propose that dual-task interference only occurs if the tasks compete for shared resources [55–57]. Neuroimaging studies have shown that dual-tasking activates regions like the prefrontal cortex (PFC) and anterior cingulate cortex, which are critical for prioritizing tasks [58, 59]. Such prioritization is often guided by the "posture first" strategy observed in healthy individuals, where stability takes precedence to avoid falls [60–62].

Neuroplastic adaptations could provide further insight into these neurocognitive deficits. CAI and LAS are associated with structural and functional brain adaptations, particularly in the sensorimotor network and regions such as the precentral gyrus, supplementary motor area, and anterior cingulate cortex. These supraspinal changes may stem from altered afferent input due to repeated injuries and impaired somatosensory feedback, which disrupt the integration of motor control signals. For example, individuals with CAI demonstrate altered corticomotor and corticospinal excitability, reflected in delayed reaction times and reduced coordination. Functional imaging studies also suggest recruitment of compensatory neural circuits in the motor cortex, underscoring the role of neuroplasticity in modulating motor control pathways. White matter microstructural changes in the cerebellum and sensorimotor integration areas further corroborate these findings [10].

In contrast, memory-related findings varied, potentially due to differences in task difficulty, sample characteristics, and methodologies. While no significant differences in standardized processing speed tests were observed, CAI patients showed slower reaction times in more ecologically valid tasks, reflecting disruptions in sensorimotor pathways and ankle proprioception. Perceptual abilities and balance performance under cognitive load were generally unaffected, but increased postural sway and altered stabilization strategies emerged in some dual-task scenarios, suggesting a context-dependent influence of cognitive demands on balance.

This review aimed to address three key research questions: (1) How is neurocognition related to ligamentous ankle injury risk? (2) How is neurocognition affected following ligamentous ankle injuries? (3) What are the differences in neurocognition between people with ligamentous ankle injuries/CAI and healthy people? Regarding the third question, individuals with CAI show deficits in attention, inhibitory control, and visual memory, compared to healthy controls and copers, with mixed findings for working memory and processing speed, while domains like language and motor skills remain unaffected. However, in relation to the first and second questions, it is important to note that while differences in neurocognitive performance between CAI patients and controls are evident, the causal direction remains unclear. It is not possible to definitively determine whether neurocognitive deficits are a consequence of ankle injuries or whether they existed prior to the injury and contributed to its occurrence. This limitation underscores the need for longitudinal studies to clarify the temporal relationship between injury and neurocognitive performance.

Clinical and Practical Implications

The findings of this review offer potential implications for the rehabilitation and management of CAI. With traditional approaches often emphasizing biomechanical and neuromuscular components, there is a growing recognition that neurocognitive factors may also play a role in the complex interplay of motor control and injury risk. While the findings highlight the relevance of neurocognitive factors in CAI, their integration into clinical practice requires careful consideration. Current evidence provides a foundation for exploring how neurocognitive deficits, such as those observed in attention, inhibitory control, and visual memory, might influence rehabilitation strategies and thus may be best applied to refine rehabilitation strategies. Incorporating targeted cognitive-motor training within rehabilitation programs could provide opportunities to address neurocognitive challenges identified in CAI patients. For example, tasks requiring divided attention, inhibitory control, or rapid decision-making could be incrementally introduced alongside traditional

exercises to better simulate the cognitive and motor demands faced during sports or daily activities. Although dual-task paradigms and neurocognitive assessments, such as the Stroop task and Flanker task, represent a step forward, it is important to recognize that these methods do not fully replicate the complexity and unpredictability of real-world demands. They serve as controlled tools to probe cognitive-motor interactions, offering insights that can inform more comprehensive rehabilitation approaches. Future research should aim to bridge the gap between laboratory-based assessments and the dynamic, high-pressure environments encountered in sports and other activities. However, the absence of significant differences in certain domains, such as language and motor skills, suggests that not all cognitive functions are equally affected. This highlights the need to consider individualized rehabilitation strategies tailored to specific neurocognitive deficits. Additionally, current definitions of LAS and CAI may not fully capture the structural complexity of ankle injuries, including possible involvement of the subtalar and midtarsal joints. Such diagnostic heterogeneity may contribute to variability in neurocognitive outcomes across studies. Future research should aim for more precise classification and consider concomitant injuries to better understand injury mechanisms and guide targeted interventions.

Limitations and Future Directions

The reviewed studies utilized a total of 27 different cognitive tasks across a variety of mono- and dual-task paradigms, which highlight the diverse approaches used to evaluate neurocognitive performance in LAS and CAI research. This heterogeneity limits direct comparisons and performing a meta-analysis. Moreover, while some of the cognitive tasks utilized in the included studies are widely used and have established validity in assessing cognitive function (e.g. CNS Vital Signs [63]) and reliability in healthy and CAI patient groups (e.g. Reactive Balance Test [64, 65]), other tasks, (e.g. Attention Training task or Catch Game Motor Planning Test), lack similar psychometric evaluation and may thus contribute to measurement variability. Developing standardized testing protocols and outcome measures, based on tests that have extensively been test for their validity and reliability in assessing cognitive function, would enable more consistent evaluations and facilitate meta-analytic synthesis in the future. Additionally, many studies did not report the raw scores or detailed performance metrics on the neurocognitive tasks themselves, which limits the transparency and reproducibility of findings. Ensuring the availability of such data in future studies would improve comparability and allow for secondary analyses. Additionally, most included studies employed cross-sectional designs, which restrict causal inferences. Future studies should adopt longitudinal designs to establish temporal relationships between neurocognitive deficits and LAS occurrence as well as CAI development, providing insights into whether these deficits are a cause or consequence of injury. A high risk of bias was noted in most studies, particularly regarding small sample sizes, inadequate blinding, and failure to adjust for confounding variables. For example, one possible concern relates to participants' educational level. Higher education levels are often associated with better cognitive functioning across multiple domains (e.g., working memory [66, 67], language skills [68], executive control [69]). However, none of the included studies controlled for level of education, which limits our ability to determine whether observed cognitive differences are attributable to CAI or to underlying differences in participants' educational backgrounds. Future research comparing the cognitive abilities of healthy individuals and ankle injury patients should take educational level into account in order to improve the accuracy and interpretability of these group differences. Another limitation of the current evidence base is the small sample size of the included studies, which leads to imprecise estimates and wide confidence intervals rather than directly increasing Type I error [25–27, 30–40]. When multiple outcomes are analyzed without correction, the risk of Type I error may increase. Six studies did not report 95% confidence intervals for group differences or effect sizes, limiting the interpretability and clinical relevance of the findings [23–25, 28, 35, 38, 42]. Future research should apply appropriate statistical controls for multiple testing and consistently report confidence intervals to improve validity and transparency. Overall, future research should focus on improving study quality by addressing these methodological shortcomings. Furthermore, the predominance of studies on young adult athletes limits generalizability to older populations or recreational athletes. Expanding research to include diverse populations would enhance the applicability of findings. Finally, while most studies focused on CAI, the neurocognitive implications of LAS remain underexplored. Research specifically examining LAS could provide a more complete understanding of the injury continuum and inform tailored interventions.

Conclusion

This review underscores the association between ligamentous ankle injuries, particularly in CAI, and neurocognitive performance. Individuals with CAI show deficits in attention, inhibitory control, and visual memory, with mixed findings for working memory and processing speed, while domains like language and motor skills remain unaffected.

While differences in neurocognitive performance between CAI patients and controls are evident, it is

uncertain whether neurocognitive deficits arise as a consequence of ankle injuries or whether they pre-exist and contribute to injury occurrence. This limitation underscores the need for longitudinal studies to establish the temporal relationship between neurocognitive performance and ligamentous ankle injuries.

Incorporating neurocognitive elements, such as dual-task training, into rehabilitation programs holds promise as a strategy to address these deficits. However, the effectiveness of such neurocognitive-focused interventions and their added value compared to conventional rehabilitation programs remain unexplored. Future research should investigate whether integrating neurocognitive components into rehabilitation can improve outcomes. Additionally, developing standardized neurocognitive testing protocols and expanding research to diverse populations will enhance the generalizability and applicability of findings.

Abbreviations

ACL	Anterior cruciate ligament
CAI	Chronic ankle instability
LAS	Lateral ankle sprain
PFC	Prefrontal cortex
PICO	Population, intervention, comparison, outcomes, and study design
PRISMA	Preferred reporting items for systematic review and meta-analyses
PROSPERO	International prospective register of systematic reviews
QUIPS	Quality In Prognostic Studies

Acknowledgements
We express our gratitude to our esteemed colleagues at the Luxembourg Institute of Research in Orthopedics, Sports Medicine and Science (LIROMS) and the Strategic Research Program Exercise and the Brain in Health & Disease: The Added Value of Human-Centered Robotics (SRP17) for their valuable insights and expertise, which significantly contributed to this research. It is worth mentioning that Bart Roelands serves as a distinguished Collen-Franqui research professor.

Author Contributions
H.C. and E.S. substantially contributed to the conception and design of the work, as well as to the acquisition, analysis and interpretation of data for the work. A.M., E.L., B.R., J.V. and B.T. substantially contributed to the conception and design of the work and the interpretation of data for the work. All authors revised the work critically for important intellectual content and gave final approval of the final version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding
Emilie Schampheleer is part of the COMET project DiMo-NEXT, which is funded by the Federal Ministry for Climate Action, Environment, Energy, Mobility, Innovation and Technology (BMK), the Federal Ministry for Labour and Economy (BMAW), and the provinces of Salzburg, Upper Austria and Tyrol within the framework of COMET – Competence Centres for Excellent Technologies. COMET is processed by The Austrian Research Promotion Agency (FFG).

Data Availability
All data generated or analyzed during this study are included in this published article.

Declarations

Ethics Approval and Consent to Participate
Hortense Corlùy, Emilie Schampheleer, Alexandre Maricot, Elke Lathouwers, Bart Roelands, Jo Verschueren, and Bruno Tassignon declare that the systematic review complies with all ethical standards. No participants were recruited for the present study, so no consent for participation needed to be collected.

Consent for Publication
Not applicable.

Competing Interests
Hortense Corlùy, Emilie Schampheleer, Alexandre Maricot, Elke Lathouwers, Bart Roelands, Jo Verschueren, and Bruno Tassignon have no competing interests of any type (i.e. financial, professional or personal) relevant to the content of this review.

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Received: 17 March 2025 / Accepted: 11 November 2025
Published online: 25 February 2026

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