Functional performance tests and return-to-sport decision-making:

Tassignon, Bruno

2021

document version
Publisher's PDF, also known as Version of record

citation for published version (APA)
Tassignon, B. (2021). *Functional performance tests and return-to-sport decision-making: Focusing on translational research with special interest in fatigue and the brain.* VUBPRESS Brussels University Press.

Functional performance tests and return-to-sport decision-making:

Focusing on translational research with special interest in fatigue and the brain.

Bruno Tassignon

Doctoral dissertation submitted in fulfilment of the requirements for the degree of Doctor in Rehabilitation Sciences and Physiotherapy at the Vrije Universiteit Brussel.

Promotors

Prof. Dr. Romain Meeusen

Prof. Dr. Evert Verhagen

VRIJE UNIVERSITEIT

Functional performance tests and return-to-sport decision-making: Focusing on translational research with special interest in fatigue and the brain.

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor
aan de Vrije Universiteit Amsterdam
en de Vrije Universiteit Brussel,
op gezag van de rectores magnifici
prof.dr. V. Subramaniam en prof.dr. C. Pauwels,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Geneeskunde
op woensdag 6 oktober 2021 om 11.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door
Bruno Tassignon
geboren te Halle, België

promotoren: prof.dr. E.A.L.M Verhagen

prof.dr. R.F. Meeusen

Total word count: 52.463

Promotors

- Prof. Dr. Romain Meeusen
  Human Physiology and Sports Physiotherapy Research Group, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel, Belgium
- Prof. Dr. Evert Verhagen
  Amsterdam Collaboration on Health and Safety in Sports, Amsterdam UMC, Department of Public and Occupational Health, Vrije Universiteit Amsterdam, The Netherlands

PhD advisory committee

- Prof. Dr. Kevin De Pauw
  Human Physiology and Sports Physiotherapy Research Group, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel, Belgium

Chair VUB – private defence

- Prof. Dr. Nele Adriaenssens
  Department of Physiotherapy, Human Physiology and Anatomy, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel, Belgium

Chair VUA – public defence

- Prof. Dr. Willem van Mechelen
  Amsterdam Collaboration on Health and Safety in Sports, Amsterdam UMC, Department of Public and Occupational Health, Vrije Universiteit Amsterdam, The Netherlands

Examination committee

- Dr. Kristel Knaepen
  Institut für Bewegungs- und Neurowissenschaft, Deutsche Sporthochschule Köln, Germany
- Prof. Dr. Erik Witvrouw
  Department of Rehabilitation Sciences, Universiteit Gent, Belgium
- Prof. Dr. David Beckwée
  Department of Physiotherapy, Human Physiology and Anatomy, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel, Belgium
- Prof. Dr. Ir. Guy Nagels
  Center for Neurosciences, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Belgium.
- Prof. Dr. Gino Kerkhoffs
  Amsterdam Collaboration on Health and Safety in Sports, Amsterdam UMC, Department of Public and Occupational Health, Vrije Universiteit Amsterdam, The Netherlands
- Prof. Dr. Willem van Mechelen
  Amsterdam Collaboration on Health and Safety in Sports, Amsterdam UMC, Department of Public and Occupational Health, Vrije Universiteit Amsterdam, The Netherlands

Table of Contents

Glossary

ACC	Accuracy
APF	Acute physical fatigue
ARC	Ankle rehabilitation checklist
ACLR	Anterior cruciate ligament reconstruction
ATFL	Anterior talofibular ligament
BMI	Body mass index
CFL	Calcaneofibular ligament
CNS	Central nervous system
CHAGS	Chamorro assisted gait scale
CAI	Chronic ankle instability
CAS	Complex adaptive systems
CI	Confidence interval
CON	Control group
EEG	Electroencephalography
FFT	Fast Fourier transform
GRRAS	Guidelines for reporting reliability and agreement studies
HSI	Hamstring strain injury
HR	Heart rate
HR-QOL	Health-related quality of life
I-PRRS	Injury-psychological readiness to return to sport scale
ICF	International classification of functioning, disability and health model
IOC	International Olympic committee
ICA	Independent component analysis
ICC	Intraclass correlation coefficient
LAS	Lateral ankle sprain

LED	Light-emitting diode
LEFS	Lower extremity functional scale
LLTQ	Lower limb task questionnaire
LORETA	Low resolution brain electromagnetic tomography
MF	Mental fatigue
M-VAS	Visual analogue scale for mental fatigue
MET	Metabolic equivalent of task
MC	Motor cortex
MDD	Minimal detectable difference
NASA-TLX	National aeronautics and space administration task load index
NICE	National institute for health and care excellence
PFC	Prefrontal cortex
PPC	Posterior parietal cortex
PROMs	Patient reported outcomes
PRISMA-P	Preferred reporting items for systematic review and meta-analysis protocols
RCT	Randomized controlled trial
RE-AIM	Reach, effectiveness, adoption, implementation, and maintenance model
RBT	Reactive balance test
RM ANOVA	Repeated measure analysis of variance
RPE	Rating of perceived exertion
RPM	Rotations per minute
RT	Reaction time
RTPa	Return to participation
RTPf	Return to performance
RTS	Return to sport
SF-36	Short form-36

SARS	Sports ankle rating system
SEM	Standard error of measurement
SEP	Standard error of prediction
SD	Standard deviation
SEBT	Star excursion balance test
SPSS	Statistical package for the social sciences
SSCI	State sport confidence inventory
StARRT	Strategic assessment of risk and risk tolerance framework
TSCI	Trait sport confidence inventory
TRIPP	Translating research into injury prevention practice framework
YBT	Y-balance test
VMRT	Visuomotor response time

Chapter 1: General introduction

Sports in the context of physical activity and health: benefits and risks

Regular physical activity has beneficial health effects at the biological, psychological and social level [1,2]. Regardless of the scientifically proven benefits of regular physical activity, sedentary behaviour, and physical inactivity are rapidly increasing worldwide [3]. Physical inactivity is currently the fourth leading risk factor for global mortality [1-3]. Consequently, both individuals and society need to invest in physical activity to improve overall biopsychosocial health. This also reduces the prevalence and incidence of physical inactivity-related diseases, illnesses, disorders and conditions, mortality rate, and high societal cost [4,5]. Nevertheless, a considerable risk of adverse events for the individual exists whilst engaging in physical activity [6-8]. Musculoskeletal injuries frequently happen during sports activities, with lower extremity injuries occurring most often [9-15]. These sports injuries have substantial repercussions at the individual and societal levels both in the short-term and long-term [6,16-22]. Therefore, participant safety during physical activity should always be the number one concern.

Mitigating the risk of musculoskeletal injuries: the role of injury risk screening

Clinicians attempt to mitigate the musculoskeletal injury risk by identifying people at risk and subsequently providing appropriate preventative strategies to achieve this objective. Injury risk screenings are typically incorporated in periodic health examinations. They contain test batteries encompassing different functional performance tests to map impairments that are associated with increased injury risk and could lead to a future injury (e.g. poor balance control). The results of this test battery are then used to compile an individualised injury risk profile.

Functional performance tests can be defined as measures of an individual's physical capacity involving multi-joint movements or postures [23,24]. Such tests often encompass simple, functional tasks (e.g. unilateral leg stance), generic movements (e.g. walking, hopping), or tasks more closely related to sport (e.g. T-agility test). However, none of the current functional performance tests can accurately predict a sports injury, and therefore no study can indeed provide evidence in favour of injury risk screening [25]. This is because individuals with high and low injury risk perform somewhat similar on these functional performance tests. Thus, making it impossible to target all individuals at high risk. In addition, functional performance tests either lack research on their clinimetric properties, and, when studied, functional performance tests mostly possess questionable clinimetric properties [23-25].

Taking into account the flaws of the current functional performance test repertoire leaves much room for improvement. There is a clear need to develop new functional performance tests relevant for injury risk screening while also carefully mapping their clinimetric properties.

Mitigating the risk of re-injury: the role of return-to-sport decision-making

In case a sports injury occurs, the clinician's goal will be to improve the patient's quality of life, let the individual return to sport/work/participation as safe and as fast as possible, to mitigate re-injury risk, and to prevent long-term sequelae.

Until 2016, the return-to-sport decision-making process and research domain were generally anecdotal and arbitrary. The first return-to-sport world consensus statement [26] was published in 2016 and established the return-to-sport process as a continuum defined by three universal phases (Return To Participation > Return-to-sport > Return To Performance). The updated Strategic Assessment of Risk and Risk Tolerance (StARRT) framework [26,27] was put forward as a holistic clinical decision model to support clinicians in their return-to-sport decision-making process. The updated StARRT framework consists of three vital steps: Assessment of Health Risk, Assessment of Activity Risk, and Risk Tolerance Assessment. The application of this framework should ultimately result in a well-informed and carefully considered decision.

Functional performance tests are deemed essential within this return-to-sport decision-making process and thus also within the StARRT framework. Their purpose is to assess re-injury risk, tissue stress and physical performance of the recovering individual. However, the current functional performance tests used in return-to-sport decision-making are largely the same that are used for injury risk screening. Hence, they have identical flaws, as mentioned earlier. Furthermore, it was communicated from the RTS consensus document that "*return-to-sport decisions should always use information gathered from a battery of tests mimicking the reactive elements and the decision-making steps athletes use in real sport situations.*" [26]. Nevertheless, the current functional performance test repertoire can be considered quite distant from the actual sport context. These tests solely involve pre-planned motor tasks without any real reactive elements and decision-making components or any contextual constraints (e.g. fatigue). Even though the purpose of these tests somewhat differs from the primary injury prevention domain, a similar call for the development and validation of new functional performance tests emerges in the return-to-sport domain.

This is important since a clear choice was made, preferring a holistic criteria-based approach when a patient advances throughout the return-to-sport continuum [26]. To progress from one phase to the next one, the patient has to pass predetermined cut-offs based on relevant questionnaires and functional performance tests. Clinicians would use this information to assess re-injury risk, evaluate residual impairments, monitor rehabilitation progress, form an impression as to whether an athlete is ready to start working towards performance enhancement, and assist the return-to-sport decision-making process [23,24,28-32]. However, research and consensus are currently lacking on return-to-sport criteria following common musculoskeletal injuries. Therefore, another key message of the 2016 consensus statement was that research and consensus are needed concerning the return-to-sport criteria for highly prevalent sports injuries [26].

Functional performance tests: lack of context and translational research?

Recently, the sports medicine and sports science fields showed an increased interest in the complexity sciences' paradigm to bridge the gap between research and clinical practice [33-45]. The first complex systems model for sports injury was suggested in 2016 and allowed our thinking to move from reductionist risk factor identification to injury pattern recognition [33]. This paper redefined how we look at injury risk, how sports injuries occur, and how we approach injuries in research and clinical practice. Of course, this correspondingly gives a different perspective on patient rehabilitation and return-to-sport decision-making.

Likewise, the application and interpretation of functional performance tests are affected by this paradigm shift. In the past, when a risk factor was exposed by one functional performance test within a test battery, a specific prevention programme was set up to target this risk factor. In this way, an attempt was made to reduce the risk of injury. Based on the complexity perspective, clinicians and researchers should view functional performance tests only as one piece of the puzzle when compiling an injury risk profile, monitoring rehabilitation progress, or making a return-to-sport decision. The results on functional performance tests should thus be interpreted in different contexts and in combination with other questionnaires and tests. This allows for functional performance testing in a context with parameters closely related to the sport (e.g. fatigue) in which potentially interesting information is embedded. Also, the inclusion of various measuring instruments over different time scales (e.g. psychological, physiological, social, biomechanical) could prove interesting in research and clinical practice.

The functional performance test domain is lacking research on the application of relevant contextual factors. Concerning contextual factors, the construct of fatigue is a ubiquitous feature of the sport (injury) context. Although no unanimous definition of fatigue in sport science exists at the mechanistic level, all can more or less agree on a general definition at the behavioural level, namely an exercise-induced decrement in performance [46-51]. In the functional performance test domain, fatigue can influence both the performance and the execution of functional performance tests in healthy and previously injured individuals [52-60]. Besides inducing performance decrements, fatigue is hypothesised to play a potential, yet controversial, role in the risk and occurrence of sports injuries [61,62]. A recent systematic review showed that fatigue could alter intrinsic modifiable injury risk factors assessed through functional performance tests, which begs the question of whether fatigue could be a useful constraint in test batteries used for injury risk screening, rehabilitation progress monitoring and return-to-sport decision-making [63]. Nevertheless, when it comes to fatigue research, all too often, clinicians have to extrapolate fundamental research findings and make assumptions towards issues or questions faced in daily clinical practice because translational research is lacking. Translational research acts as a bridge between science and clinical practice by researching fundamental outcomes linked to a clinical context. Therefore, lots of progress can still be made at the translational research level. For instance, clinicians often use functional performance tests and can only observe the results at the behavioural level. It could thus be of interest to them how different fatigue types affect functional test performance and alter underlying physiological and psychological outcomes.

Rationales, aims and outline of this thesis

This PhD thesis's overall purpose is to contribute to clinical decision-making and functional performance testing across the sports injury spectrum. The research line of this PhD thesis is carried out in light of the background above. The three specific objectives of this thesis encompass:

(1) establishing scientifically sound criteria to substantiate return-to-sport decisions following lateral ankle sprains,

(2) mapping the reliability characteristics of a new neurocognitive functional performance test: the reactive balance test,

(3) exploring electrophysiological brain changes induced by various fatigue types when participants performed the Y-balance test and reactive balance test.

Based upon the 2016 return-to-sport consensus statement, both research and agreement are needed concerning the return-to-sport criteria for highly prevalent sports injuries. Researchers and clinicians working with athletes who suffered an anterior cruciate ligament injury [64-70] or hamstring strain injury [31,71-75] have already undertaken steps to develop this relatively new criteria-based approach. However, for other common sports injuries, like lateral ankle sprain injuries, such endeavours remain to be undertaken. Lateral ankle sprains are among the most frequently incurred musculoskeletal injuries in individuals participating in recreational and competitive sports [76-82]. The recurrence rate of a lateral ankle sprain (LAS) injury is one of the highest amongst all musculoskeletal injuries [83-89], while many individuals who incur a LAS injury develop chronic ankle instability (CAI) [90-92]. In the long term, CAI can initiate the onset of post-traumatic osteoarthritis and ultimately culminate in biopsychosocial impairments [93-95]. From a clinical perspective, return-to-sport decisions following LAS injury are typically informed by fundamental research and anecdotal evidence, combined with the clinician's experience and clinical reasoning skills. In most cases, an emphasis is placed on returning to the sport as fast as possible, with the time to return-to-sport being treated as a proxy of rehabilitation success. However, such an approach seems to be highly ineffective, given the recurrence rate of LAS injuries. This high recurrence rate is hypothesised to be mainly caused by the increased re-injury risk and premature return-to-sport clearance. The increased re-injury risk has to be viewed in light of sensorimotor impairments' persistence due to previous LAS injury. Premature return-to-sport clearance happens due to the lack of scientifically supported return-to-sport criteria, questionnaires and tests [88,96-100]. Therefore, I aim to identify objective return-to-sport criteria for individuals who incurred a lateral ankle sprain injury through a systematic review in **Chapter 2**, whilst also extracting relevant questionnaires, clinical tests, and functional performance tests during the systematic search process.

In **Chapter 3**, another central concern of the sports injury domain is addressed, namely the need to develop and validate functional performance tests to support injury risk screening, monitor rehabilitation progress and guide return-to-sport decision-making. My colleagues and I cross-referenced the scientific literature, the extensive reviews on lower extremity functional performance test by Hegedus and colleagues [23,24] and the inventory of functional performance tests that were produced during the systematic search process of the previous chapter. The two most important observations from this exercise were as follows. Firstly, despite the return-to-sport consensus statement emphasising "a battery of tests mimicking the reactive elements and the decision-making steps athletes use in real sport situations", none of the encountered functional performance tests encompassed reactive elements or decision-making steps athletes use in real sport situations. Secondly, most functional performance tests have not been sufficiently researched in terms of clinimetric properties (e.g. reliability, validity) [23, 24]. Even though one of the suggested key drivers for safe and effective sports performance is a person's ability to adapt to various changing conditions [101], an apparent absence of functional performance tests integrating adaptability exists. The Star Excursion Balance Test (SEBT) and Y-balance test (YBT) are two related tests that have been investigated extensively and have consistently shown good reliability and criterion validity within the current functional performance testing repertoire. This partially led to these tests' success, given the tests' ability to reliably assess injury risk and its associated claim to predict lower extremity injuries [24,102,103]. One of the possibilities to measure adaptability in a clinician-friendly way is by adding neurocognitive components (e.g. visuomotor response time, decision-making) to existing functional performance tests. Building on the strong foundations of the YBT, we added neurocognitive (decision-making components) and adaptability (reactive elements) features in order to bring the YBT closer to the sports context, and thereby creating a new functional performance test in our lab: the reactive balance test (RBT) [104]. An additional rationale substantiating the development of such neurocognitive functional performance tests can be derived from the association between poorer neurocognitive performance and increased lower extremity sports injury risk [105-107]. Nevertheless, before this new functional performance test could be implemented in scientific research or clinical practice, its basic clinimetric properties should be mapped. Therefore, I plan to assess several reliability characteristics of the reactive balance test in Chapter 3.

In the subsequent phase of the project (Chapter 4 & 5), the aim is to contribute to the lack of contextual factors and the need for translational research within the functional performance test domain. I address this research vacuum by inducing different lab-controlled fatigue types in healthy individuals performing the traditional YBT and the new RBT. Simultaneously, underlying (electro)physiological changes at the brain level will be explored when participants perform these two functional performance tests.

In **Chapter 4**, I focus on the mental fatigue side of the fatigue spectrum. In other words, how extended exhaustive cognitive effort interacts with these two functional balance tests. Mental fatigue can be defined as a psychobiological state that emerges during or after periods of prolonged cognitive activity [108]. Fundamental research already showed that mental fatigue interferes with human balance control and increases the probability of losing balance [109,110]. These findings further substantiate the increasing body of scientific evidence that indicates that the brain's neocortex is essential in human balance control [111,112]. Nevertheless, the construct of balance has commonly been represented in these studies by technical outcome measures that provide little to no direct support for the understanding or changing methodology and interpretation for clinicians in their daily clinical practice [109-112]. Therefore, it could be valuable to integrate commonly used functional performance tests that aim to measure balance control in research. This will bridge the gap between the lab and clinical practice, and directly supports clinicians. Therefore, the aim is to research how mental fatigue would interact with the YBT and RBT whilst measuring electrophysiological data at the brain level through electroencephalography.

Chapter 5 explores a different side of the fatigue spectrum by letting participants perform a 30-second all-out cycling protocol to induce acute physical fatigue. In sports science, acute physical fatigue is defined as a behavioural state resulting in exercise-induced performance decrements [49,51]. Acute physical fatigue can occur during, at the end or after exercise performance and emerges from a multitude of interactions between underlying peripheral and central physiological changes, psychological variables and the environment [46-51]. Conflicting results in SEBT and YBT performance have been found when participants are exposed to acute physical fatigue [56-60,113]. At the same time, most research measuring electrophysiological brain activity during balance tasks is limited to bipedal or single leg stance and stepping or walking tasks [111]. This implies that these results are difficult to translate and apply to specific functional performance tests (i.e. YBT) utilised in clinical practice. Therefore, the purpose of this chapter is to research how acute physical fatigue would interact with the YBT and RBT whilst measuring electrophysiological data at the brain level through electroencephalography.

Chapter 6 discusses the main findings from the combined research studies with the strengths and limitations of this research project. I also devote attention to the studies' practical implications and potential future perspectives for research. The general conclusion is outlined at the end of this chapter.

References

1. Crooke R, Haseler C, Haseler T, Collins J, Crockett A. Physical activity and moving more for health. *J R Coll Physicians Edinb.* 2020;50(2):173-180.
2. WHO Guidelines Approved by the Guidelines Review Committee. In: *Global Recommendations on Physical Activity for Health.* Geneva: World Health Organization. Copyright © World Health Organization 2010.; 2010.
3. Ozemek C, Lavie CJ, Rognmo Ø. Global physical activity levels - Need for intervention. *Prog Cardiovasc Dis.* 2019;62(2):102-107.
4. Bueno DR, Marucci Mde F, Codogno JS, Roediger Mde A. [The costs of physical inactivity in the world: a general review]. *Cien Saude Colet.* 2016;21(4):1001-1010.
5. Ding D, Kolbe-Alexander T, Nguyen B, Katzmarzyk PT, Pratt M, Lawson KD. The economic burden of physical inactivity: a systematic review and critical appraisal. *Br J Sports Med.* 2017;51(19):1392-1409.
6. Garrick JG, Requa RK. Sports and Fitness Activities: The Negative Consequences. *JAAOS - Journal of the American Academy of Orthopaedic Surgeons.* 2003;11(6).
7. Franklin BA, Billecke S. Putting the benefits and risks of aerobic exercise in perspective. *Current sports medicine reports.* 2012;11(4):201-208.
8. Verhagen E, Bolling C, Finch CF. Caution this drug may cause serious harm! Why we must report adverse effects of physical activity promotion. In: *Br J Sports Med.* Vol 49. England2015:1-2.
9. Andreoli CV, Chiaramonti BC, Buriel E, Pochini AC, Ejnisman B, Cohen M. Epidemiology of sports injuries in basketball: integrative systematic review. *BMJ Open Sport Exerc Med.* 2018;4(1):e000468.
10. Kilic O, Kemler E, Gouttebarge V. The "sequence of prevention" for musculoskeletal injuries among adult recreational footballers: A systematic review of the scientific literature. *Physical therapy in sport : official journal of the Association of Chartered Physiotherapists in Sports Medicine.* 2018;32:308-322.
11. Fu MC, Ellenbecker TS, Renstrom PA, Windler GS, Dines DM. Epidemiology of injuries in tennis players. *Curr Rev Musculoskelet Med.* 2018;11(1):1-5.
12. Patel DR, Yamasaki A, Brown K. Epidemiology of sports-related musculoskeletal injuries in young athletes in United States. *Transl Pediatr.* 2017;6(3):160-166.
13. Kilic O, Maas M, Verhagen E, Zwerver J, Gouttebarge V. Incidence, aetiology and prevention of musculoskeletal injuries in volleyball: A systematic review of the literature. *European journal of sport science.* 2017;17(6):765-793.
14. Browne GJ, Barnett P. Common sports-related musculoskeletal injuries presenting to the emergency department. *J Paediatr Child Health.* 2016;52(2):231-236.
15. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J Athl Train.* 2007;42(2):311-319.

16. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012;380(9859):2163-2196.
17. Gribble PA, Bleakley CM, Caulfield BM, et al. 2016 consensus statement of the International Ankle Consortium: prevalence, impact and long-term consequences of lateral ankle sprains. *Br J Sports Med.* 2016;50(24):1493-1495.
18. Grice A, R. KS, G. CP. Nonelite exercise-related injuries: Participant reported frequency, management and perceptions of their consequences. *Scandinavian Journal of Medicine & Science in Sports.* 2014;24(2):e86-e92.
19. Ruiz AL, Kelly M, Nutton RW. Arthroscopic ACL reconstruction: a 5-9 year follow-up. *The Knee.* 2002;9(3):197-200.
20. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med.* 2007;35(10):1756-1769.
21. Wilk KE, Arrigo CA. Rehabilitation: Common Problems and Solutions. *Clin Sports Med.* 2018;37(2):363-374.
22. Finch C, Owen N, Price R. Current injury or disability as a barrier to being more physically active. *Med Sci Sports Exerc.* 2001;33(5):778-782.
23. Hegedus EJ, McDonough S, Bleakley C, Cook CE, Baxter GD. Clinician-friendly lower extremity physical performance measures in athletes: a systematic review of measurement properties and correlation with injury, part 1. The tests for knee function including the hop tests. *Br J Sports Med.* 2015;49(10):642-648.
24. Hegedus EJ, McDonough SM, Bleakley C, Baxter D, Cook CE. Clinician-friendly lower extremity physical performance tests in athletes: a systematic review of measurement properties and correlation with injury. Part 2-the tests for the hip, thigh, foot and ankle including the star excursion balance test. *Br J Sports Med.* 2015;49(10):649-656.
25. Bahr R. Why screening tests to predict injury do not work-and probably never will...: a critical review. *Br J Sports Med.* 2016;50(13):776-780.
26. Ardern CL, Glasgow P, Schneiders A, et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med.* 2016;50(14):853-864.
27. Shrier I. Strategic Assessment of Risk and Risk Tolerance (StARRT) framework for return-to-play decision-making. *British Journal of Sports Medicine.* 2015;49(20):1311-U1340.
28. Hegedus EJ, McDonough S, Bleakley C, et al. Physical performance tests predict injury in National Collegiate Athletic Association athletes: a three-season prospective cohort study. *Br J Sports Med.* 2016;50(21):1333-1337.
29. Chimera NJ, Warren M. Use of clinical movement screening tests to predict injury in sport. *World Journal of Orthopedics.* 2016;7(4):202-217.

30. Gomez-Piqueras P, Gonzalez-Rubio J, Sainz de Baranda P, Najera A. Use of functional performance tests in sports: Evaluation proposal for football players in the rehabilitation phase. *Turk J Phys Med Rehab.* 2018;64(2):148-154.
31. Mendiguchia J, Martinez-Ruiz E, Edouard P, et al. A Multifactorial, Criteria-based Progressive Algorithm for Hamstring Injury Treatment. *Med Sci Sports Exerc.* 2017;49(7):1482-1492.
32. Ljungqvist A, Jenoure P, Engebretsen L, et al. The International Olympic Committee (IOC) Consensus Statement on periodic health evaluation of elite athletes March 2009. *Br J Sports Med.* 2009;43(9):631-643.
33. Bittencourt NFN, Meeuwisse WH, Mendonca LD, Nettel-Aguirre A, Ocarino JM, Fonseca ST. Complex systems approach for sports injuries: moving from risk factor identification to injury pattern recognition-narrative review and new concept. *Br J Sports Med.* 2016;50(21):1309- 1314.
34. Bekker S, Clark AM. Bringing complexity to sports injury prevention research: from simplification to explanation. In: *Br J Sports Med.* Vol 50. England2016:1489-1490.
35. Cook C. Predicting future physical injury in sports: it's a complicated dynamic system. In: *Br J Sports Med.* Vol 50. England2016:1356-1357.
36. Glazier PS. Towards a Grand Unified Theory of sports performance. *Hum Mov Sci.* 2017;56(Pt A):139-156.
37. Gokeler A, Verhagen E, Hirschmann MT. Let us rethink research for ACL injuries: a call for a more complex scientific approach. In: *Knee Surg Sports Traumatol Arthrosc.* Vol 26. Germany2018:1303-1304.
38. Harbourne RT, Stergiou N. Movement variability and the use of nonlinear tools: principles to guide physical therapist practice. *Phys Ther.* 2009;89(3):267-282.
39. Hulme A, Finch CF. From monocausality to systems thinking: a complementary and alternative conceptual approach for better understanding the development and prevention of sports injury. *Inj Epidemiol.* 2015;2(1):31.
40. Stergiou N, Decker LM. Human movement variability, nonlinear dynamics, and pathology: is there a connection? *Hum Mov Sci.* 2011;30(5):869-888.
41. Sturmberg JP, Martin CM, Katerndahl DA. Systems and complexity thinking in the general practice literature: an integrative, historical narrative review. *Ann Fam Med.* 2014;12(1):66-74.
42. Vaz DV, Silva PL, Mancini MC, Carello C, Kinsella-Shaw J. Towards an ecologically grounded functional practice in rehabilitation. *Hum Mov Sci.* 2017;52:117-132.
43. Balague N, Torrents C, Hristovski R, Kelso JA. Sport science integration: An evolutionary synthesis. *Eur J Sport Sci.* 2017;17(1):51-62.
44. Pol R, Hristovski R, Medina D, Balague N. From microscopic to macroscopic sports injuries. Applying the complex dynamic systems approach to sports medicine: a narrative review. *Br J Sports Med.* 2018.
45. Verhagen E, van Dyk N, Clark N, Shrier I. Do not throw the baby out with the bathwater; screening can identify meaningful risk factors for sports injuries. *Br J Sports Med.* 2018.

46. Enoka RM, Duchateau J. Muscle fatigue: what, why and how it influences muscle function. *J Physiol.* 2008;586(1):11-23.
47. Marcora SM. Do we really need a central governor to explain brain regulation of exercise performance? *Eur J Appl Physiol.* 2008;104(5):929-931; author reply 933-925.
48. Gibson AS, Swart J, Tucker R. The interaction of psychological and physiological homeostatic drives and role of general control principles in the regulation of physiological systems, exercise and the fatigue process - the integrative governor theory. *European journal of sport science.* 2018;18(1):25-36.
49. Lambert EV, Gibson AS, Noakes TD. Complex systems model of fatigue: integrative homoeostatic control of peripheral physiological systems during exercise in humans. *Br J Sports Med.* 2005;39(1):52-62.
50. Meeusen R, Roelands B. Fatigue: Is it all neurochemistry? *Eur J Sport Sci.* 2018;18(1):37-46.
51. Knicker AJ, Renshaw I, Oldham ARH, Cairns SP. Interactive processes link the multiple symptoms of fatigue in sport competition. *Sports Med.* 2011;41(4):307-328.
52. Gustavsson A, Neeter C, Thomee P, et al. A test battery for evaluating hop performance in patients with an ACL injury and patients who have undergone ACL reconstruction. *Knee Surgery Sports Traumatology Arthroscopy.* 2006;14(8):778-788.
53. Borotikar BS, Newcomer R, Koppes R, McLean SG. Combined effects of fatigue and decision making on female lower limb landing postures: Central and peripheral contributions to ACL injury risk. *Clinical Biomechanics.* 2008;23(1):81-92.
54. Bruce O, Moull K, Fischer S. Principal components analysis to characterise fatigue-related changes in technique: Application to double under jump rope. *Journal of Sports Sciences.* 2017;35(13):1300-1309.
55. Collins JD, Almonroeder TG, Ebersole KT, O'Connor KM. The effects of fatigue and anticipation on the mechanics of the knee during cutting in female athletes. *Clinical Biomechanics.* 2016;35:62-67.
56. Baghbani F, Woodhouse LJ, Gaeini AA. Dynamic postural control in female athletes and nonathletes after a whole-body fatigue protocol. *Journal of Strength and Conditioning Research.* 2016;30(7):1942-1947.
57. McMullen KL, Cosby NL, Hertel J, Ingersoll CD, Hart JM. Lower Extremity Neuromuscular Control Immediately After Fatiguing Hip-Abduction Exercise. *Journal of Athletic Training.* 2011;46(6):607-614.
58. Zech A, Steib S, Hentschke C, Eckhardt H, Pfeifer K. Effects of localized and general fatigue on static and dynamic postural control in male team handball athletes. *J Strength Cond Res.* 2012;26(4):1162-1168.
59. Whyte E, Burke A, White E, Moran K. A high-intensity, intermittent exercise protocol and dynamic postural control in men and women. *J Athl Train.* 2015;50(4):392-399.

60. Johnston W, Dolan K, Reid N, Coughlan GF, Caulfield B. Investigating the effects of maximal anaerobic fatigue on dynamic postural control using the Y-Balance Test. *Journal of science and medicine in sport.* 2018;21(1):103-108.

61. Benjaminse A, Webster KE, Kimp A, Meijer M, Gokeler A. Revised approach to the role of fatigue in anterior cruciate ligament injury prevention: a systematic review with meta-analyses. *Sports Med.* 2019;49(4):565-586.

62. Bourne MN, Webster KE, Hewett TE. Is Fatigue a Risk Factor for Anterior Cruciate Ligament Rupture? *Sports Med.* 2019;49(11):1629-1635.

63. Verschueren J, Tassignon B, De Pauw K, et al. Does Acute Fatigue Negatively Affect Intrinsic Risk Factors of the Lower Extremity Injury Risk Profile? A Systematic and Critical Review. *Sports Med.* 2020;50(4):767-784.

64. Dingenen B, Gokeler A. Optimization of the Return-to-Sport Paradigm After Anterior Cruciate Ligament Reconstruction: A Critical Step Back to Move Forward. *Sports Med.* 2017;47(8):1487-1500.

65. Rambaud AJM, Ardern CL, Thoreux P, Regnaux JP, Edouard P. Criteria for return to running after anterior cruciate ligament reconstruction: a scoping review. *Br J Sports Med.* 2018.

66. Gokeler A, Welling W, Zaffagnini S, Seil R, Padua D. Development of a test battery to enhance safe return to sports after anterior cruciate ligament reconstruction. *Knee Surgery Sports Traumatology Arthroscopy.* 2017;25(1):192-199.

67. Grindem H, Snyder-Mackler L, Moksnes H, Engebretsen L, Risberg MA. Simple decision rules can reduce reinjury risk by 84% after ACL reconstruction: the Delaware-Oslo ACL cohort study. *Br J Sports Med.* 2016;50(13):804-808.

68. Herbst E, Hoser C, Hildebrandt C, et al. Functional assessments for decision-making regarding return to sports following ACL reconstruction. Part II: clinical application of a new test battery. *Knee Surgery Sports Traumatology Arthroscopy.* 2015;23(5):1283-1291.

69. Kyritsis P, Bahr R, Landreau P, Miladi R, Witvrouw E. Likelihood of ACL graft rupture: not meeting six clinical discharge criteria before return to sport is associated with a four times greater risk of rupture. *Br J Sports Med.* 2016;50(15):946-951.

70. Rambaud AJM, Semay B, Samozino P, et al. Criteria for Return to Sport after Anterior Cruciate Ligament reconstruction with lower reinjury risk (CR'STAL study): protocol for a prospective observational study in France. *BMJ Open.* 2017;7(6):e015087.

71. van der Horst N, van de Hoef S, Reurink G, Huisstede B, Backx F. Return to Play After Hamstring Injuries: A Qualitative Systematic Review of Definitions and Criteria. *Sports Med.* 2016;46(6):899-912.

72. Hickey JT, Timmins RG, Maniar N, Williams MD, Opar DA. Criteria for Progressing Rehabilitation and Determining Return-to-Play Clearance Following Hamstring Strain Injury: A Systematic Review. *Sports Med.* 2017;47(7):1375-1387.

73. Shrier I, Serner A, Wangensteen A, Steele RJ, Weir A. Measuring heterogeneity of reinjury risk assessments at the time of clearance to return to play: A feasibility study. *J Sci Med Sport.* 2017;20(3):255-260.
74. van der Horst N, Backx F, Goedhart EA, Huisstede BM. Return to play after hamstring injuries in football (soccer): a worldwide Delphi procedure regarding definition, medical criteria and decision-making. *Br J Sports Med.* 2017;51(22):1583-1591.
75. Zambaldi M, Beasley I, Rushton A. Return to play criteria after hamstring muscle injury in professional football: a Delphi consensus study. *Br J Sports Med.* 2017;51(16):1221-1226.
76. Doherty C, Delahunt E, Caulfield B, Hertel J, Ryan J, Bleakley C. The Incidence and Prevalence of Ankle Sprain Injury: A Systematic Review and Meta-Analysis of Prospective Epidemiological Studies. *Sports Medicine.* 2014;44(1):123-140.
77. Drakos MC, Domb B, Starkey C, Callahan L, Allen AA. Injury in the national basketball association: a 17-year overview. *Sports Health.* 2010;2(4):284-290.
78. Fong DTP, Hong YL, Chan LK, Yung PSH, Chan KM. A systematic review on ankle injury and ankle sprain in sports. *Sports Medicine.* 2007;37(1):73-94.
79. Jacobs CL, Hincapie CA, Cassidy JD. Musculoskeletal injuries and pain in dancers: a systematic review update. *J Dance Med Sci.* 2012;16(2):74-84.
80. Waterman BR, Owens BD, Davey S, Zacchilli MA, Belmont PJ. The Epidemiology of Ankle Sprains in the United States. *Journal of Bone and Joint Surgery-American Volume.* 2010;92A(13):2279-2284.
81. Wolfenden HEG, Angioi M. Musculoskeletal Injury Profile of Circus Artists A Systematic Review of the Literature. *Medical Problems of Performing Artists.* 2017;32(1):51-59.
82. Cumps E, Verhagen E, Meeusen R. Prospective epidemiological study of basketball injuries during one competitive season: Ankle sprains and overuse knee injuries. *Journal of Sports Science and Medicine.* 2007;6(2):204-211.
83. Beynnon BD, Murphy DF, Alosa DM. Predictive factors for lateral ankle sprains: A literature review. *Journal of Athletic Training.* 2002;37(4):376-380.
84. Bahr R, Bahr IA. Incidence of acute volleyball injuries: A prospective cohort study of injury mechanisms and risk factors. *Scandinavian Journal of Medicine & Science in Sports.* 1997;7(3):166-171.
85. Gribble PA, Bleakley CM, Caulfield BM, et al. Evidence review for the 2016 International Ankle Consortium consensus statement on the prevalence, impact and long-term consequences of lateral ankle sprains. *British Journal of Sports Medicine.* 2016;50(24):1496-+.
86. Swenson DM, Yard EE, Fields SK, Comstock RD. Patterns of Recurrent Injuries Among US High School Athletes, 2005-2008. *American Journal of Sports Medicine.* 2009;37(8):1586-1593.
87. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: Summary and recommendations for injury prevention initiatives. *Journal of Athletic Training.* 2007;42(2):311-319.

88. Malliaropoulos N, Ntessalen M, Papacostas E, Longo UG, Maffulli N. Reinjury After Acute Lateral Ankle Sprains in Elite Track and Field Athletes. *American Journal of Sports Medicine.* 2009;37(9):1755-1761.
89. Konradsen L, Bech L, Ehrenbjerg M, Nickelsen T. Seven years follow-up after ankle inversion trauma. *Scandinavian Journal of Medicine & Science in Sports.* 2002;12(3):129-135.
90. Delahunt E, Coughlan GF, Caulfield B, Nightingale EJ, Lin CWC, Hiller CE. Inclusion Criteria When Investigating Insufficiencies in Chronic Ankle Instability. *Medicine and Science in Sports and Exercise.* 2010;42(11):2106-2121.
91. Hertel J. Functional anatomy, pathomechanics, and pathophysiology of lateral ankle instability. *Journal of Athletic Training.* 2002;37(4):364-375.
92. Hiller CE, Kilbreath SL, Refshauge KM. Chronic Ankle Instability: Evolution of the Model. *Journal of Athletic Training.* 2011;46(2):133-141.
93. Harrington KD. Degenerative arthritis of the ankle secondary to long standing lateral ligament instability. *J Bone Joint Surg.* 1979;61A:354-361.
94. Landeros O, Frost HM, Higgins CC. Post traumatic anterior ankle instability. *Clin Orthop.* 1968;56:169-178.
95. Al-Mahrouqi MM, Macdonald DA, Vicenzino B, Smith MD. Physical Impairments in Adults With Ankle Osteoarthritis: A Systematic Review and Meta-analysis. *Journal of Orthopaedic & Sports Physical Therapy.* 2018;48(6):449-+.
96. Steib S, Zech A, Hentschke C, Pfeifer K. Fatigue-Induced Alterations of Static and Dynamic Postural Control in Athletes With a History of Ankle Sprain. *Journal of Athletic Training.* 2013;48(2):203-208.
97. McKay GD, Goldie PA, Payne WR, Oakes BW. Ankle injuries in basketball: injury rate and risk factors. *British Journal of Sports Medicine.* 2001;35(2):103-108.
98. Boyce SH, Quigley MA, Campbell S. Management of ankle sprains: a randomised controlled trial of the treatment of inversion injuries using an elastic support bandage or an Aircast ankle brace. *British Journal of Sports Medicine.* 2005;39(2):91-96.
99. McKay G, Goldie P, Payne WR, Oakes BW, Watson LF. A prospective study of injuries in basketball: A total profile and comparison by gender and standard of competition. *Journal of Science and Medicine in Sport.* 2001;4(2):196-211.
100. van der Wees PJ, Hendriks EJM, Jansen MJ, van Beers H, de Bie RA, Dekker J. Adherence to physiotherapy clinical guideline acute ankle injury and determinants of adherence: a cohort study. *Bmc Musculoskeletal Disorders.* 2007;8:7.
101. Glasgow P, Bleakley CM, Phillips N. Being able to adapt to variable stimuli: the key driver in injury and illness prevention? *Br J Sports Med.* 2013;47(2):64-65.
102. Gribble PA, Hertel J, Plisky P. Using the star excursion balance test to assess dynamic postural-control deficits and outcomes in lower extremity injury: a literature and systematic review. *J Athl Train.* 2012;47(3):339-357.

103. Plisky PJ, Gorman PP, Butler RJ, Kiesel KB, Underwood FB, Elkins B. The reliability of an instrumented device for measuring components of the star excursion balance test. *North American journal of sports physical therapy : NAJSPT.* 2009;4(2):92-99.

104. Verschueren J, Tassignon B, Pluym B, Van Cutsem J, Verhagen E, Meeusen R. Bringing context to balance: development of a reactive balance test within the injury prevention and return to sport domain. *Arch Physiother.* 2019;9(6):eCollection 2019.

105. Wilkerson GB, Mokha M. Neurocognitive reaction time predicts lower extremity sprains and strains. *IJATT.* 2012;17(6):4-9.

106. Swanik CB, Covassin T, Stearne DJ, Schatz P. The relationship between neurocognitive function and noncontact anterior cruciate ligament injuries. *American Journal of Sports Medicine.* 2007;35(6):943-948.

107. Herman DC, Barth JT. Drop-Jump Landing Varies With Baseline Neurocognition: Implications for Anterior Cruciate Ligament Injury Risk and Prevention. *American Journal of Sports Medicine.* 2016;44(9):2347-2353.

108. Van Cutsem J, Marcora S, De Pauw K, Bailey S, Meeusen R, Roelands B. The effects of mental fatigue on physical performance: a systematic review. *Sports Med.* 2017;47(8):1569-1588.

109. Lew FL, Qu XD. Effects of mental fatigue on biomechanics of slips. *Ergonomics.* 2014;57(12):1927-1932.

110. Qu X, Xie Y, Hu X, Zhang H. Effects of Fatigue on Balance Recovery From Unexpected Trips. *Human factors.* 2019:18720819858794-18720819858794.

111. Wittenberg E, Thompson J, Nam CS, Franz JR. Neuroimaging of Human Balance Control: A Systematic Review. *Frontiers in human neuroscience.* 2017;11:170-170.

112. Surgent OJ, Dadalko OI, Pickett KA, Travers BG. Balance and the brain: A review of structural brain correlates of postural balance and balance training in humans. *Gait & posture.* 2019;71:245-252.

113. Armstrong R, Brogden CM, Milner D, Norris D, Greig M. The Influence of Fatigue on Star Excursion Balance Test Performance in Dancers. *Journal of Dance Medicine & Science.* 2018;22(3):142-147.

Chapter 2: Criteria-based return to sport decision-making following lateral ankle sprain injury: a systematic review and narrative synthesis.

Bruno Tassignon
Jo Verschueren
Eamonn Delahunt
Michelle Smith
Bill Vicenzino
Evert Verhagen
Romain Meeusen

Sports Med (2019), 49, pp. 601–619.

Abstract

Objective

To identify prospective studies that used a criteria-based return to sport (RTS) decision-making process for patients with lateral ankle sprain (LAS) injury.

Design

Systematic review and narrative synthesis.

Data sources

PubMed (MEDLINE), Web of Science, PEDro, Cochrane Library, SPORTDiscus (EBSCO), ScienceDirect, and Scopus were searched till 23 November 2018.

Eligibility criteria for selecting studies

Studies were included if they prospectively applied a criteria-based RTS decision-making process for patients with LAS injury. Studies were excluded if they merely gathered outcome measures at the RTS time-point. Studies were also excluded if patients were recovering from ankle fracture, high ankle sprain, medial ankle sprain, chronic ankle instability or complex ankle injury.

Results

No studies were identified which used a criteria-based RTS decision-making process for patients with LAS injury. We were unable to conduct a quantitative synthesis or meta-analysis, so we provide a narrative synthesis of relevant questionnaires, as well as clinical and functional assessments commonly used in studies retrieved in the search.

Conclusion

There are currently no published evidence-based criteria to inform RTS decisions for patients with a LAS injury. Based upon our narrative synthesis we propose a number of variables that could be used to develop a criteria-based RTS decision paradigm. Future research should aim to reach consensus on these variables and apply them to actual RTS decisions within prospective study designs. Furthermore, we suggest that complex systems theory and the return to sport continuum could be used to inform the development of a RTS decision-making paradigm for athletes with LAS injury.

Key points

1) No published evidence-based criteria exist to inform return to sport decisions for patients following lateral ankle sprain injury.
2) Return to sport decisions following lateral ankle sprain injury are generally time-based.
3) We propose that complex systems theory and the return to sport continuum could be used to inform the development of a criteria-based return to sport paradigm to bridge the gap between research and clinical practice.

Background

Lateral ankle sprains are one of the most frequently incurred musculoskeletal injuries in individuals participating in recreational and competitive sports [1-7]. During the 12-month time period following a first-time lateral ankle sprain (LAS) injury, athletes have a significantly increased risk of reinjury (risk ratio in the first six months after first-time LAS = 9.8; risk ratio from 6 months up to 1 year after first-time LAS = 5.6) in comparison to athletes who have never incurred a LAS injury [8-10]. The recurrence rate of LAS injury is one of the highest amongst all musculoskeletal injuries [10-14]. A high proportion of individuals who incur a LAS injury develop chronic ankle instability (CAI) [15-17], which can initiate the onset of post-traumatic osteoarthritis and ultimately culminate in the development of both physical and psychological impairments [18-20].

In 2012, evidence-based clinical guidelines published by Kerkhoffs and colleagues [21] identified that a wide variety of efficacious treatment options exist for individuals with an acute LAS injury. In spite of this, LAS injury is still typically regarded as an innocuous injury and, even today, individuals with an acute LAS injury do not consistently seek or receive appropriate medical treatment and patient-centred rehabilitation [22-25]. Recently, an update of these evidence-based clinical guidelines (2018) [26] recommended that in order to facilitate a faster return to sport (RTS) for individuals with an acute LAS injury, clinicians should implement a multi-faceted exercised-based rehabilitation programme (e.g. proprioception, strength, coordination) [26,27].

Clinically, LAS injury management and RTS decisions are typically informed by fundamental and anecdotal evidence, as well as the experience and clinical reasoning of the clinician who is managing the injury. Oftentimes an emphasis is placed on an expedient return to activity, with the time to RTS being used as a surrogate measure of rehabilitation success. However, such an approach can be counterproductive, as evidenced by the high recurrence rate of LAS injuries. This high recurrence rate is hypothesised to be mainly caused by an increased reinjury risk due to previous LAS, the persistence of sensorimotor impairments and premature RTS clearance [13,22,28-31]. Therefore, there is a need to develop and implement evidence-based progressive rehabilitation programmes, as well as specific evidence-based criteria to guide RTS decisions for individuals with acute LAS injury.

To initiate the development of a criteria-based RTS decision paradigm for acute LAS injury patients, variables, cut-offs and ranges of criteria to be included in this paradigm need to be determined and evaluated. Injury-specific criteria-based RTS decision paradigms exist for anterior cruciate ligament reconstruction (ACLR) and hamstring strain injury (HSI); these have been informed by critical [32], scoping [33] and systematic reviews [34,35].

To our knowledge, no systematic reviews have been published on the topic of criteria-based RTS decision-making for individuals with acute LAS injury. Therefore, the aim of this systematic review was to identify and discuss the results of prospective studies that used a criteria-based RTS decision-making process for patients with acute LAS injury, with the objective of identifying suitable criteria to inform this complex clinical process.

Methods

The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) and developed in line with the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P) [36]. The review protocol can be accessed via PROSPERO:

(http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017060910) [37].

Information sources

PubMed (MEDLINE), Web of Science, PEDro, Cochrane Library, SPORTDiscus (EBSCO), ScienceDirect, and Scopus were searched to collate published articles from the dates of inception of these databases to 23 November 2018.

Eligibility criteria

Studies were included if they prospectively applied a criteria-based RTS decision-making process for patients (adults aged > 18 years) who had incurred a LAS injury. Studies that merely gathered outcome measures at the time-point that corresponded to RTS were excluded. RTS-criteria encompassed any criteria that were used to guide the RTS decision-making processes [38]. LAS injury was defined in accordance with the definition advocated by the International Ankle Consortium; "*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*" [15,39-41]. Studies were excluded if patients were recovering from ankle fracture, high ankle sprain, medial ankle sprain, CAI or complex ankle injury.

Search strategy

The search strategy was developed by two authors (BT, JV) and encompassed three term sets that were combined with 'AND'. The term sets included words for ankle injuries (e.g. "ankle injuries" or "ankle sprain"), criteria and tests (e.g. "test", "measurement" or "criteria"), and outcomes (e.g. "return to sport", "match fitness"). The words within each term were separated by 'OR'. The specialised and detailed search strategy for each database can be found in *Electronic Supplementary Material Table S1*. Return to work and return to duty were deemed beyond the scope of this review and were not included in the systematic search strategy. Reference lists of included articles, relevant reviews and meta-analyses were screened to identify possible additional articles.

Study selection and assessment of risk of bias

All databases were searched by one author (BT). Next, all retrieved titles, abstracts, full texts and citations were aggregated in the Rayyan web application (https://rayyan.qcri.org) [42]. Publications were independently screened for inclusion by two authors (BT, JV) using a staged process of reviewing titles and abstracts, and eventually reviewing the remaining full texts. Only published articles in peer-reviewed journals were considered for full text inclusion. If no full text was available, corresponding authors were contacted. If no full text could be supplied after contacting the corresponding authors, the full text was ordered via the library of the Vrije Universiteit Brussel. Inclusion and exclusion decisions were recorded via the Rayyan web app. Differences in the decision to include or exclude articles were settled through discussion. If agreement could not be reached through discussion, a third author (RM) was consulted in order to reach consensus. Depending on the design of study, appropriate checklists for the assessment of risk of bias were selected: Cochrane Collaboration's tool (RCT) and NICE guidelines (wide scope of study designs).

Data extraction and synthesis

To answer the research question, questionnaires and tests for which the outcome was a priori identified as an RTS criterion by the original studies were extracted from included full texts. Furthermore, when screening abstracts and full texts, two authors (BT, JV) systematically extracted questionnaires, clinical and functional tests and criteria in ankle sprain populations, to build a test inventory used in ankle sprain populations. These extracted measures did not have to be linked to RTS, but were collated to give an indication of objective rehabilitation parameters in LAS. For studies included in the systematic review, criteria that were used to make the RTS decision were defined as cut-off values or ranges that were applied to the corresponding questionnaires and tests (e.g. limb symmetry index ≥ 90% on a single leg hop for distance test).

Results

Study collection

A total of 948 articles were identified and screened for inclusion using title and abstract. After exclusion of non-relevant articles (n = 915), 33 full text articles were assessed for eligibility and their reference lists checked for possible additional relevant articles. Finally, no studies could be included in this systematic review, as not one prospective study using a criteria-based RTS decision-making approach for patients who had incurred a LAS injury was retrieved. The selection process can be found in ***Figure 1***.

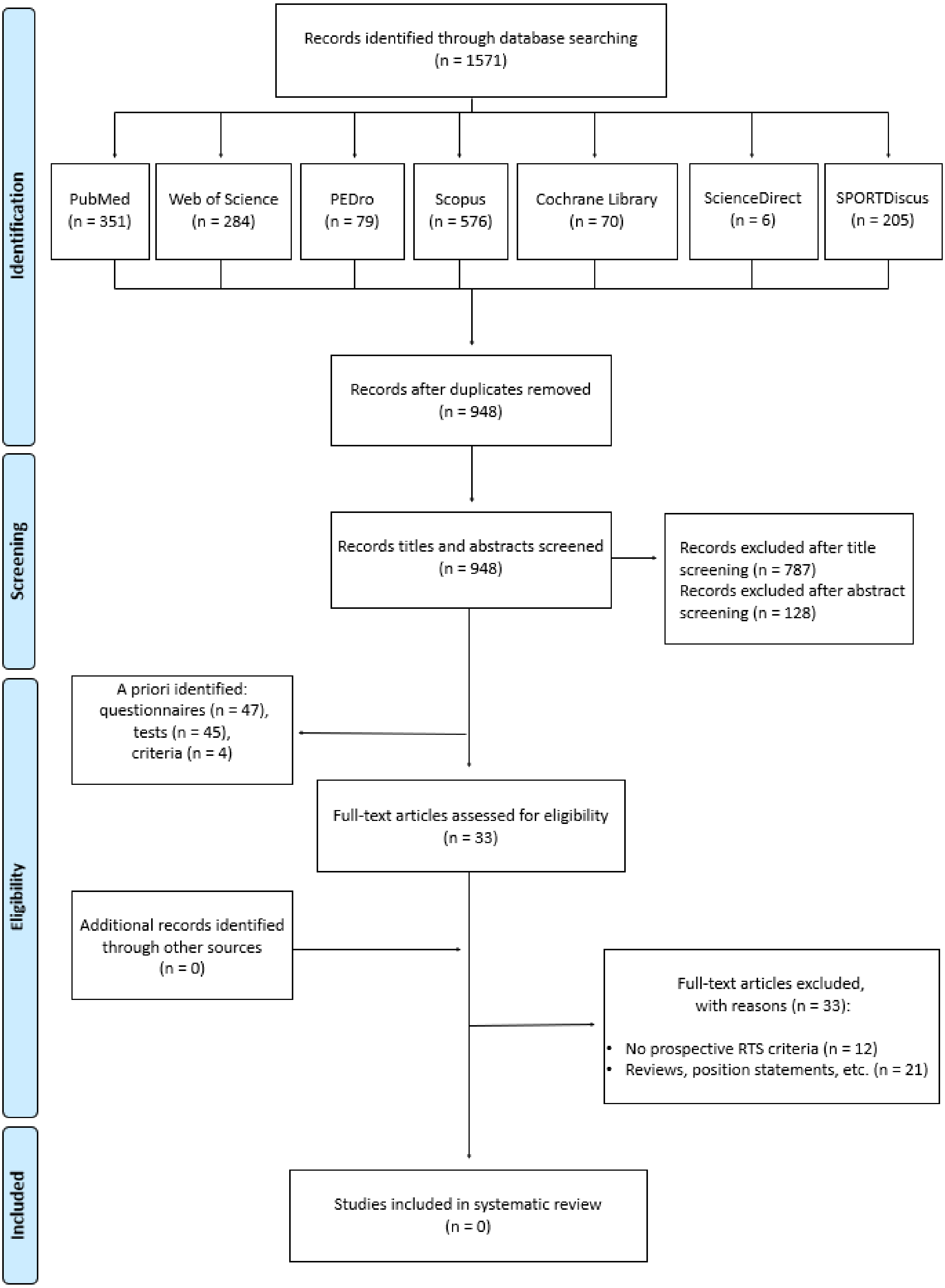

Figure 1 – flowchart: RTS = Return to sport

Test inventory created during the data collection and extraction processes

A total of forty-seven questionnaires, forty-five clinical assessment measures and/or functional performance tests, as well as four criteria that were used in ankle sprain, LAS, mechanical ankle instability and functional ankle instability populations were identified during the screening of abstracts and full texts, prior to the inclusion of studies in the systematic review.

Questionnaires

In total 37 questionnaires were extracted from the reviews by Haywood et al (2004) [43], Donahue et al. (2011) [44], Simon et al. (2014) [45], Jia et al. (2017) [46], and the study by Da Cunha et al (2016) [47]. We recommend that readers who are interested in implementing patient-reported outcome measures questionnaires for ankle injury patients should consult these papers. Furthermore, seven additional questionnaires [Ankle Rehabilitation Checklist (ARC) [48], Chamorro Assisted Gait Scale (CHAGS) [49], Health-Related Quality of Life (HR-QOL) [50,51], Lower Extremity Functional Scale (LEFS) [52,53], Lower Limb Task Questionnaire (LLTQ) [54], Sports Ankle Rating System (SARS) [55,56], and Short Form-36 (SF-36) [50,57-59]] were identified.

Two narrative reviews [60,61] suggested the use of questionnaires to measure psychological readiness to return to sport (n = 3), namely: the Injury-Psychological Readiness to Return to Sport Scale (I-PRRS) [62], Trait Sport Confidence Inventory (TSCI) [63,64], and State Sport Confidence Inventory (SSCI) [64]. However, no prospective studies were identified which used psychological readiness to return to sport after acute LAS injury as a primary or secondary outcome measure.

Clinical assessment measures and functional performance tests

A wide spectrum of clinical assessment measures and functional performance tests were reported for evaluating an ankle sprain, and a patient's rehabilitation progress and physical performance. An overview of these tests with their corresponding references can be found in the *Electronic Supplementary Material Tables S2 and S3*.

Clinical assessment measures for ankle sprains were assigned to the following categories: swelling (n = 1), ligamentous laxity (n = 7), and range of motion (n = 2). For the functional performance tests, we identified the following categories: proprioception (n = 1), hopping and jumping (n = 14), range of motion (n = 1), balance (n = 6), agility/speed (n = 9), and strength (n = 4). Even though an extensive range of clinical assessment measures and functional performance tests were identified, no consistency in their use across studies could be identified. Some important gaps in the testing spectrum were identified, as some constructs remain to be investigated (e.g. movement quality). These will be discussed in section 4.2.3, bullet point 5, and section 4.3.

Criteria

Only one study applied a set of criteria to determine acceptable RTS [65]. These criteria encompassed a limb symmetry index (≥ 80% to compare the injured and un-injured limbs) when performing both a triple forward hop for distance and a triple lateral hop for distance, an absence of pain and no loss of function rated on 10-point scales. These criteria were not used to determine whether an ankle sprain patient was ready to RTS or not, but rather to give the patient an acceptable or unacceptable RTS score after six weeks and six months when the patient had already resumed his or her sport. Given this time-contingent RTS decision, this study was excluded from the systematic review, with the result that no studies could be included to answer the research question.

Discussion

Since the predetermined research question could not be answered due to a lack of available literature, a narrative synthesis was written to address: (1) the use of the outcome "time to return to play, sport or work", (2) rationales and considerations for RTS decision-making following LAS injury, and (3) directions for future research. The objective of this narrative synthesis was to aid the building of a solid base for objective, evidence-founded, scalable, safe, and sustainable RTS decisions for athletes with an acute LAS injury. The inventory of reported tests (*Electronic Supplementary Material Tables S2 and S3*) identified across studies was used alongside the general findings from the data collection and extraction phases to substantiate these suggestions.

Use of the outcome "time to return to play, sport or work"

The outcome time to return to sport, work or play was frequently represented amongst the screened articles [66-78]. Based on the extensive use of this outcome [66-78] and the lack of prospectively determined RTS criteria throughout the ankle sprain injury literature, it is reasonable to infer that ankle rehabilitation, both in clinical practice as well as research, is still firmly anchored in time-contingent protocols and decision-making. This underscores the need to develop phase-sensitive and specific RTS assessment clusters and criteria in order to help clinicians determine which athlete is ready to proceed to a certain RTS phase and which athlete is not. In addition to assessing rehabilitation progress and performance, these assessment clusters and criteria should give clinicians insight into the athletes' re-injury risk [8-10,79,80]. It is important to not confound the phases of rehabilitation with phase dependent criteria. The phases of rehabilitation are often tailored to injury and the phases of tissue repair, and mainly include goalsetting, therapy content and tests to monitor the progression of the patient. Phase dependent criteria, however, are tailored to the athlete and not always in line with these phases of rehabilitation, and mainly serve the purpose to support clinicians in making RTS decisions. In the ACLR [32,33,81-85] and HSI [34,35,86-89] domains, researchers and clinicians are currently undertaking steps to develop this relatively new criteria-based approach. Therefore, it is logical that such an approach should be developed for LAS injury patients.

Rationales and considerations for RTS decision-making following acute LAS injury

Is it time to implement complex systems theory into the RTS decision-making paradigm?

Recently, the fields of sports medicine and sport science have shown an increased reinterest in the complexity sciences' paradigm in order to bridge the gap between research and clinical practice [90-102]. An interesting feature of complex adaptive systems (CAS) is that studying or collecting discrete variables, components or sub-parts of CAS does not automatically lead to the understanding of the emergent behaviour at a higher level of such systems. To put it in the words of Douglas Adams: "*If you try and take a cat apart to see how it works, the first thing you have on your hands is a nonworking cat*" [103]. In living systems, a multi-level hierarchical organisation is suggested where various processes operating across different time scales dynamically interact in nonlinear ways and lead to the emergence of new components and properties through self-organisation [99,100]. This is why patients can and should also be considered as CAS [104]. For example, patients with a perfectly recovered ankle without any residual complaints but high fear of reinjury could be delayed in resuming their sport, while patients with some residual complaints and better coping skills might RTS sooner.

Since athletes and patients can be considered as CAS [104], decision-making models with a reductionist approach might not be suited to substantiate sustainable and responsible decisions along the RTS continuum. Moreover, making RTS decisions is both a complex and complicated affair due to the many intrinsic (e.g. risk factors, physiology, coping strategy) and extrinsic (e.g. social support, playing position, stakeholders) variables interacting with each other at different time scales (e.g. molecular, organism and social levels) via both bottom-up and top-down processes. The goal of complexity research is to focus on a more holistic approach, with the objective of determining how these constraints interact with and influence the emergent behaviour of the patient. The International Classification of Functioning, Disability and Health model, the Strategic Assessment of Risk and Risk Tolerance (StARRT) framework and the concept of patient-centred care align with this complexity paradigm as they focus on the individual, its sub-systems and interactions with the environment, and not solely on the injured body tissue. Concentrating on LAS injury research, complexity science has only been evaluated in an implicit form and is not currently being explicitly explored. One article suggested the use of a constraint led approach to better understand and treat LAS patients [105], while other studies have applied some (mainly non-linear) complexity principles in LAS [106-110] and CAI [111-115] populations.

This implies that both research and clinical practice are currently continuing the evolution towards a more holistic view on rehabilitation and that we are gradually moving away from deterministic concepts and models of risk, and reductionistic assessment. It also necessitates the further development of phase-sensitive and -specific multifactorial assessments and decision-making models that accommodate these insights and are based on the interactions of their components in order to create a dynamic RTS clearance profile for each patient. Eventually, this adaptable RTS clearance profile could be used by clinicians to allow each patient to make safe and evidence-informed phase-transitions along the RTS continuum. If we consider an

RTS decision model after acute LAS injury as a CAS, the RTS decision would be the emergence of behaviour based on the interactions of multiple factors (e.g. questionnaires, clinical assessments and functional tests, stakeholders) that are both dynamic and temporal by nature. This supports the use of complex systems theory throughout the RTS decision-making paradigm.

Defining the RTS continuum

First and foremost, distinct and well-described phases have to be demarcated along the RTS continuum in order to build a dynamic RTS decision-making model that guides clinicians through the rehabilitation journey. Therefore, we adopted the continuum and definitions from the 2016 Consensus statement on RTS [38]:

1. Return to participation (RTPa): the athlete may be participating in rehabilitation, training (modified or unrestricted), or in sport, but at a level lower than his or her RTS goal. The athlete is physically active, but not yet 'ready' (medically, physically and/or psychologically) to RTS. It is possible to train to perform, but this does not automatically mean RTS.
2. Return to sport (RTS): the athlete has returned to his or her defined sport but is not performing at his or her desired performance level. Some athletes may be satisfied with reaching this stage, and this can represent successful RTS for that individual.
3. Return to performance (RTPf): this extends upon the RTS phase. The athlete has returned to his or her defined sport and is performing at or above his or her pre-injury level. For some athletes this stage may be characterised by personal best performance or expected personal growth as it relates to performance.

For an injured athlete to be able to successfully RTPf, all stakeholders (athlete, medical staff, coaches, etc.) should participate actively in managing the dynamic, but delicate, balance between rehabilitation, training and re-injury prevention. Therefore, the shared RTS management and decision-making processes should combine aspects of clinical and psychological state, risk and performance assessment along the continuum and emerge in a dynamic RTS clearance profile. Therefore, we advocate the use of the definitions of the consensus statement in future research and clinical practice instead of the ambiguous return to play/activity/work outcomes.

Which variables can we consider for building a dynamic RTS clearance profile?

Shrier and colleagues (2014) performed an exploratory study on the differences in professionals' (clinicians and non-clinicians) opinions about which criteria should be used to guide RTS decisions and who is best able to evaluate these decisions [116]. They concluded that both injury-related and non-injury-related risk assessment criteria should be included and that non-clinicians (e.g. coaches) should participate actively in the RTS decision-making process. We advocate that injury-related and non-injury related variables should be considered in the development of a criteria-based RTS decision-making paradigm for acute LAS injury patients.

- Time to return to full activity coupled to grading of the LAS injury: a thing of the past?

Historically, acute LAS injuries have been categorized in terms of severity by a three-tiered grading system [117]. A grade I LAS injury is characterized by some torn ligamentous fibres with negligible haemorrhage. Normally, no ligamentous laxity or residual instability is present [118,119]. A grade II, or moderate, LAS injury involves an incomplete tear of the ligament with subsequent mild ligamentous laxity and residual instability, minor reduction in function, possible decrease in strength, and the potential for loss of proprioception [118]. A grade III, or severe, LAS injury is characterized by complete rupture of the ligament with substantial ligamentous laxity and concomitant instability, and possibly a complete loss of function, strength, and proprioception [117,120-122]. Textbooks published between the 1950s and 1990s suggested time frames to RTS based on the severity (or grade) of the injury (i.e. up to 12 days for a grade I injury , 2 – 6 weeks for a grade II injury and up to 26 weeks for a grade III injury) [117-122]. While these time-contingent return to activity statements provided clinicians with an estimate as to when athletes could return to activity, we consider that these are outdated and do not reflect the clinical symptoms, resolution of impairments nor the ability of the athlete.

A 2014 study on time to RTS in high school athletes observed that a 95% probability exists for full return to sports participation within 10 days after a first-time ankle sprain injury [123]. However, an even more recent study (2018) reported that individuals who sustained a LAS injury still exhibit increased ankle ligamentous laxity, reduced self-reported function, restriction of dorsiflexion range of motion, and impaired dynamic postural balance at the RTS time-point (mean ± standard deviation = 12.7 ± 10.0 days) [124]. Consequently, these authors suggested that athletes with a LAS injury require more extensive care to resolve impairments before they should be allowed to RTS [124]. This is a 'wake-up call' for researchers and clinicians to develop and implement criteria-based RTS decisions following acute LAS injury in order to reduce the number of patients who RTS with residual impairments and to decrease the risk of reinjury. We therefore advocate that time should not be included as a variable in a dynamic criteria-based RTS decision framework. However, we do acknowledge that time to RTS will always be present in the background, since the RTS team (e.g. athlete, medical staff, coaches) desires the athlete to RTS as fast as possible.

- Predisposing factors increasing the (re)injury risk and prognostic factors increasing the risk of developing CAI

We will briefly summarize the most relevant modifiable risk factors, both intrinsic and extrinsic, that can aid clinicians in assessing an individual's risk of LAS (re)injury. Concerning intrinsic risk factors for (re)injury, clinicians should be attentive to reduced ankle dorsiflexion range of motion [125-127], decreased proprioception, reduced static and dynamic postural balance [126,128-136], poor neuromuscular control and running technique (high plantar pressure during running) [135,137], reduced ankle muscle strength [126,132,134,138], reduced cardio-respiratory endurance [135] and delayed peroneus brevis reaction time [134]. These intrinsic modifiable risk factors could be targeted by the appropriate prescription of exercises. Concerning extrinsic risk factors, clinicians should be cognisant of type of sport (e.g. basketball, volleyball) [3,5,139], position played (e.g. centre in basketball) [140,141], athlete exposure [3,5,139], landing after a jump [9,139], stepping on an opponent's foot [142], and playing surface [143-145]. While some of these extrinsic risk factors are potentially modifiable, it is highly unlikely that many of them would be altered (e.g. changing a player's field position). Nevertheless, these extrinsic risk factors may have a role in the RTS decision-making process (e.g. volleyball athlete vs. long-distance runner).

Since up to 40% of individuals who incur a first-time LAS injury will develop CAI within a 1-year time-frame [146], it is important for clinicians to identify possible prognostic factors for developing CAI. These encompass: inability to perform a jump-landing (drop land or drop vertical jump) within 2 weeks after first-time LAS injury [26], impaired postural balance [146,147], impaired lower limb kinematics [146,148], increased ankle laxity after 8 weeks [149,150], and lower perceived activities of daily living function [146]. Integrating these insights in rehabilitation may be important to prevent the development of CAI.

Clinicians should be aware of these interacting factors and act accordingly throughout rehabilitation. For a complete overview of risk factors and prognostic factors, we suggest the recent published consensus statement (2018) on the diagnosis, treatment and prevention of ankle sprains [26].

- Ligament healing, ankle laxity and arthrokinematics

The anterior talofibular ligament (ATFL) and calcaneofibular ligament (CFL) are the most commonly injured ankle ligaments and tissue damage of these ligaments can result in ankle joint laxity and arthrokinematics alterations [151,152]. To check ligament healing, ankle laxity and arthrokinematics, clinicians often use the same clinical assessment measures they use for grading the LAS injury. Ligament healing is distinctly demarcated into inflammatory (3 – 5 days), proliferative (3 – 21 days), and remodelling (14 – 28 days) phases [153]. However, the exact time an ankle ligament needs to heal and when/if ankle laxity is resolved after an acute LAS injury is unknown. Significant improvements in mechanical stability are often observed from six weeks to three months post-injury, but mechanical laxity remains present in a vast number of patients [70]. Remarkably, recovery of mechanical laxity does not coincide with the 'end' of the remodelling phase, nor do either of these coincide with the aforementioned typical timeframe of RTS (10 to 12 days post-injury). Even though some theoretical hypotheses exist on this matter, this discrepancy is still poorly understood. Moreover, mechanical laxity and the characteristic features of CAI remain present up to 1-year in a significant subset of individuals who have incurred a LAS injury, even upon RTS [70,154]. Since ligament damage is associated with mechanical and sensorimotor changes, it is important to obtain an impression of ligament healing via relevant clinical assessment measures (e.g. anterior drawer, talar tilt, posterior talar glide test) [154-156]. However, ligament damage is not limited only to the talocrural joint. Despite the lack of consistency in scientific literature, one could consider the subtalar joint and the other foot joints, as these can also contribute to LAS injury and the development of CAI [135,157,158]. Even though impairments in ankle joint arthrokinematics are regularly identified in individuals with CAI, clinical assessment measures have limited predictive value for CAI when conducted in the acute phase of a first-time LAS injury [159]. However, if increased ankle laxity following first-time LAS is still present after 8 weeks, there is an increased risk of developing CAI [149,150]. Therefore, we advocate the utilisation of clinical assessments of ankle ligamentous laxity and support their inclusion in a multifactorial criteria-based RTS decision framework.

- Clinical tests and patient reported outcomes (PROMs): application of the 2019 consensus statement and recommendations of the International Ankle Consortium [156]

For the assessment of ankle pain (e.g. Numeric Pain Rating Scale, Foot and Ankle Disability Index), swelling (e.g. figure of eight test), range of motion (e.g. weight-bearing lunge tests, goniometer, inclinometer), muscle strength (e.g. hand-held dynamometry) and PROMs (e.g. Foot and Ankle Disability Index, Foot and Ankle Ability Measure), we refer to this consensus statement [156]. The authors built their recommendations on scientific evidence and after completion of a modified Delphi process [156]. We advocate including these suggested components into the criteria-based RTS decision paradigm, as they gather information on the initial state of the CAS and can be used to evaluate the efficacy of the treatment implemented, monitor the progress of the patient, and guide the rehabilitation process.

- Functional and sport-specific performance tests

For high-performance athletes, sport and athlete analyses are warranted to determine relevant functional and sport-specific tests to guide rehabilitation and RTS. Subsets of these analyses should contain the sport-specific exercise physiological profile, biomechanical profile (e.g. kinetics, kinematics, movement sequences of relevant movement patterns), muscle-tendon functioning profile (e.g. energy absorption, energy transfer), and skill profile (e.g. environment stability, size of the movement). In light of different requirements, this will be unique for each sport. For example, a football player will have different, as well as some overlapping, needs in all four subsets when compared to a marathon runner.

The rationale for the use of functional performance tests is to assess possible impairments that need to be addressed in rehabilitation and to form an impression as to whether an athlete is ready to start working towards performance enhancement [160-162]. Such tests often encompass more generic movements (e.g. walking, hopping) or simpler tasks (e.g. unilateral leg stance) than sport-specific tests. The main goal of sport-specific tests (e.g. reactive agility, linear speed) is to measure the athlete's current performance level and provide performance-specific training goals for both the athlete and the coaching staff. Quantitative and/or qualitative impairments of the human movement system can also be identified during sport-specific tests and used to guide the rehabilitation process.

In individuals with LAS injury and CAI, impairments are exposed during static (e.g. balance error scoring system, foot lift test) and dynamic (e.g. star excursion balance test) postural balance tests and hopping [147,163-171]. Bilateral deficits in postural balance have been observed following acute unilateral LAS injury, suggesting a central impairment in neuromuscular control and supporting the hypothesis of central nervous system (CNS) reorganization as a contributing mechanism to persistent neuromuscular deficits [172]. Recent research has shown that alterations in movement strategies during simple (e.g. walking, single limb stance) and more difficult tasks (e.g. dynamic balance, drop vertical jump, hopping) are present immediately and six months after an acute LAS and in CAI populations [109,112,147,148,163,173-182]. These alterations in sensorimotor control might reduce an athlete's ability to adequately react, adapt or respond to unexpected external stimuli [183,184], as is the case in open skill sports. Therefore, it is warranted to further explore and implement various "new" motor learning methods in rehabilitation (e.g. constraints led approach, differential training, contextual interference). These methods, which consider the complexity of the sensorimotor system, have been shown to be more beneficial than traditional motor learning methods (e.g. repetitive practice, methodological series of exercises) for injury prevention, rehabilitation and performance training [185-190].

Furthermore, as higher injury rates have been reported towards the end of a game [140], fatigue should also be considered and utilized within the functional and sport-specific testing paradigm as part of the RTS decision-making process. Fatigue during exercise or sport competition manifests itself in multiple ways (e.g. decrease in performance, alteration of movement patterns, slower decision-making) and is the result of multiple and complex interactions of both bottom-up and top-down processes [191]. Therefore, it can also be considered as a constraint interacting with the injured sensorimotor system. Clinicians can use various kinds of fatigue (e.g. peripheral fatigue, mental fatigue) to challenge the human movement system [191-195].

These insights highlight the importance of functional and sport-specific testing of athletes after LAS injury with consideration of the CAS nature of the sensorimotor system. In summary, we suggest the use of:

a. Quantitative performance analysis.
b. Movement quality assessment evaluating generic and sport-specific movement focusing both on end result performance and on applied movement strategy.
c. Acute fatigue as a constraint and extra criterion in performance testing.

- Load monitoring (the acute:chronic workload ratio)

In light of evidence that poor load management is a major threat for athletes to develop an injury [196], the International Olympic Committee (IOC) published a two-part consensus statement on load in sport and risk of injury and illness [196,197]. They provided practical guidelines to manage load in sport to enable practitioners to prescribe scientifically founded training and competition loads. These guidelines provide suggestions about how to monitor training, competition and psychological load, athlete well-being, and injury. Poor load management can either mean exposing an athlete to loads that are too high, thus increasing the risk of (re)injury, or exposing an athlete to loads that are too low and do not prepare him/her for when RTS or RTPf clearance is given [198]. This was suggested and visualised in the workload-injury aetiology model by Windt and Gabbett (2016) [199]. Therefore, the calculation of the acute:chronic workload ratio throughout the RTS decision-making process is advised as it permits clinicians to quantify a player's risk of subsequent injury [200], and to monitor training loads so training errors and unfavourable fatigue can be avoided.

- Psychological and psychosocial factors

The importance of psychological factors for a successful RTS has been proven in the ACLR domain [201-203]. Readiness to RTS after ACLR was most affected by fear of reinjury, emotional disturbance, and lack of motivation, self-esteem, confidence in the injured limb, locus of control and self-efficacy [201-203]. Two narrative reviews on RTS after LAS [60,61] suggest the use of questionnaires to measure psychological readiness to return to sport, specifically the Injury-Psychological Readiness to Return to Sport Scale (I-PRRS) [62], Trait Sport Confidence Inventory (TSCI) [63,64], and State Sport Confidence Inventory (SSCI) [64]. While direct evidence to support the role of these psychological and psychosocial factors is currently lacking, general insights support them. Therefore, we advise the inclusion of the assessment of psychological and psychosocial factors as variables in the dynamic criteria-based RTS decision paradigm after LAS injury.

We advise readers to consult the narrative review by Podlog and colleagues (2014) on the psychosocial factors in sports injury rehabilitation and RTS [204] and invite researchers in the sport science domain to start collaborating with or further involve psychologists in the multidisciplinary domain of RTS following LAS injury.

- Decision modifying variables

To support the CAS nature of a RTS decision, the authors would like to suggest that the following variables could be added to the dynamic criteria-based RTS decision framework: quality of the communication and consensus of opinion between all stakeholders, stress [205], sleep [206], socio-economic status of the athlete [116], social support of the athlete (e.g. family, friends, fans) [204], risk of injury to team members or opponents [116], and short-term and long-term financial burden [116]. Note that the inclusion or exclusion of some variables (e.g. socio-economic status, financial burden) would result in a more idealistic versus a more realistic perspective on the RTS decision clearance profile. All of the aforementioned variables need to be considered when developing a dynamic RTS clearance profile, with each variable having its own calculated weight whilst interacting with the other determined RTS variables. To our knowledge, the main variables have been discussed above, although we would like to invite researchers, clinicians, coaches, athletes and students to further complement these variables in order to gain further insights and to build a more comprehensive model.

- Summary

We have identified clinical, functional, sport specific, psychosocial and decision modifying variables as part of the RTS decision paradigm. Inclusion of a time contingent approach in this RTS decision paradigm is not advised.. The weight of each variable can change as the patient moves through the RTS continuum. For instance, the weight of sport-specific tests may be less in the dynamic RTS clearance profile when making RTPa decisions but will be of great importance when considering RTS or RTPf decisions. Future research should try to determine relevant interactions, the weight of each variable in the RTS decision matrix, and objective criteria to make correct RTS decisions following acute LAS injury.

The authors would like to suggest a phenomenological framework and components for a dynamic RTS decision-making paradigm along the RTS continuum (see Figures 2 and 3). With respect to content (questionnaires, tests, criteria), no suggestions will be formulated since there is no rigorous evidence to fill in this framework. Hopefully, the aforementioned rationales and considerations for building a dynamic criteria-based RTS decision-making paradigm can inspire researchers, clinicians and trainers. Assuming control theory as a metaphor, four general requirements have to be met for the control of any system (even a dynamic system for decision-making): (1) there has to be a goal (the goal condition = RTPf), (2) one has to be able to determine the state of the system (the observability condition = biopsychosocial assessment), (3) it has to be possible to affect the state of the system (the action condition = the athlete or patient), and (4) there needs to be a model of the system (the model condition = RTS clearance profile) [207]. Before such a dynamic criteria-based RTS decision-making paradigm can be created, consensus on its variables needs to be found among clinicians, researchers and coaches.

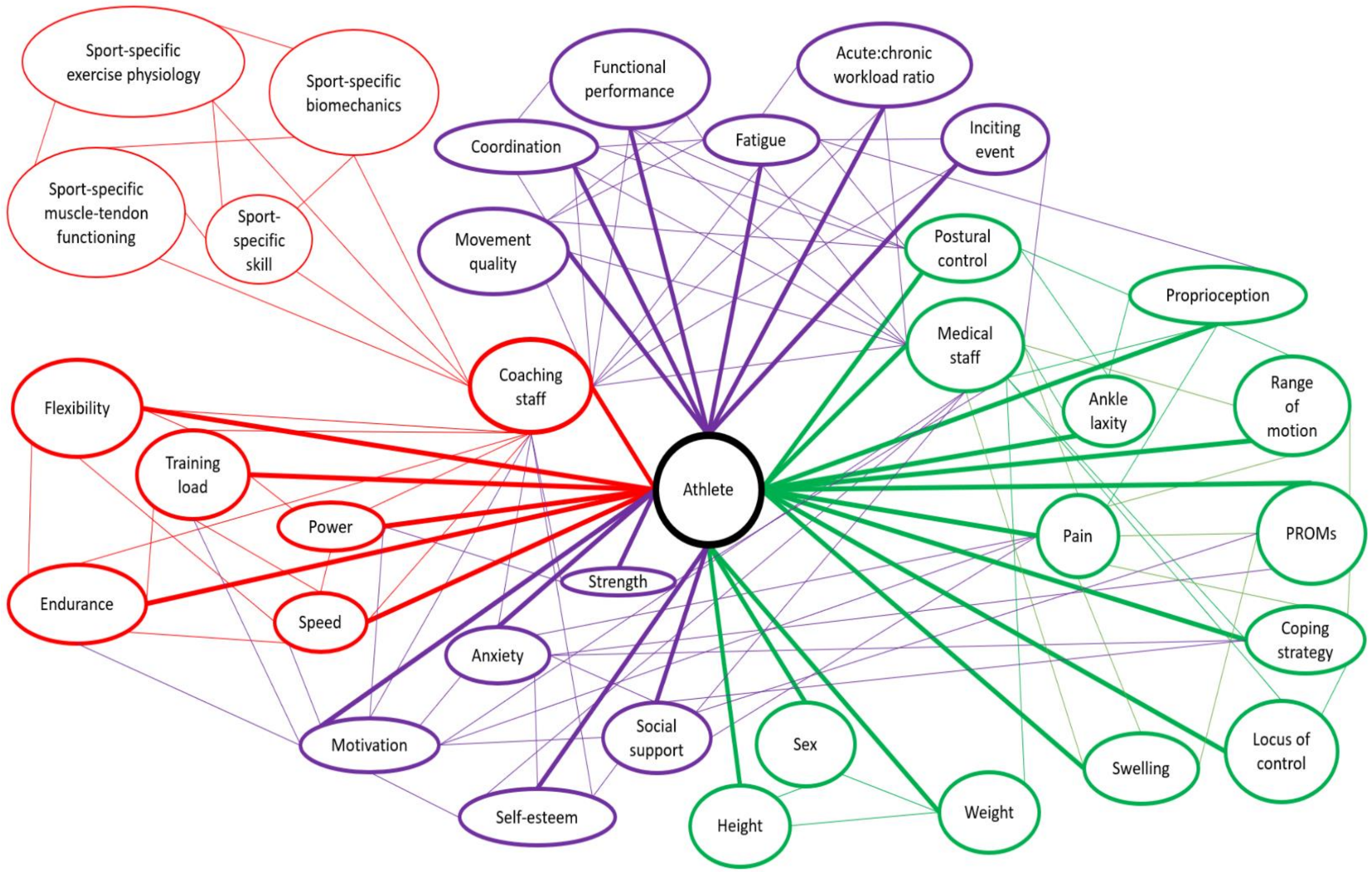

Figure. 2 – Example of a dynamic RTS profile: note that most of the variables discussed in section 4.2.3 were inserted. Thick lines indicate variables directly related to the athlete. Such a profile would further depict possible correlations and interactions between variables (= thin lines). The emergence of a RTPa, RTS, RTPf decision can arise due to the dynamic and nonlinear changes in and interactions between these constantly fluctuating variables. Colours are an illustration of possible variables related to a certain stakeholder group (green = medical staff; red = coaching staff; purple = medical and coaching staff). RTPa = Return to participation; RTS = Return to sport; RTPf = Return to performance.

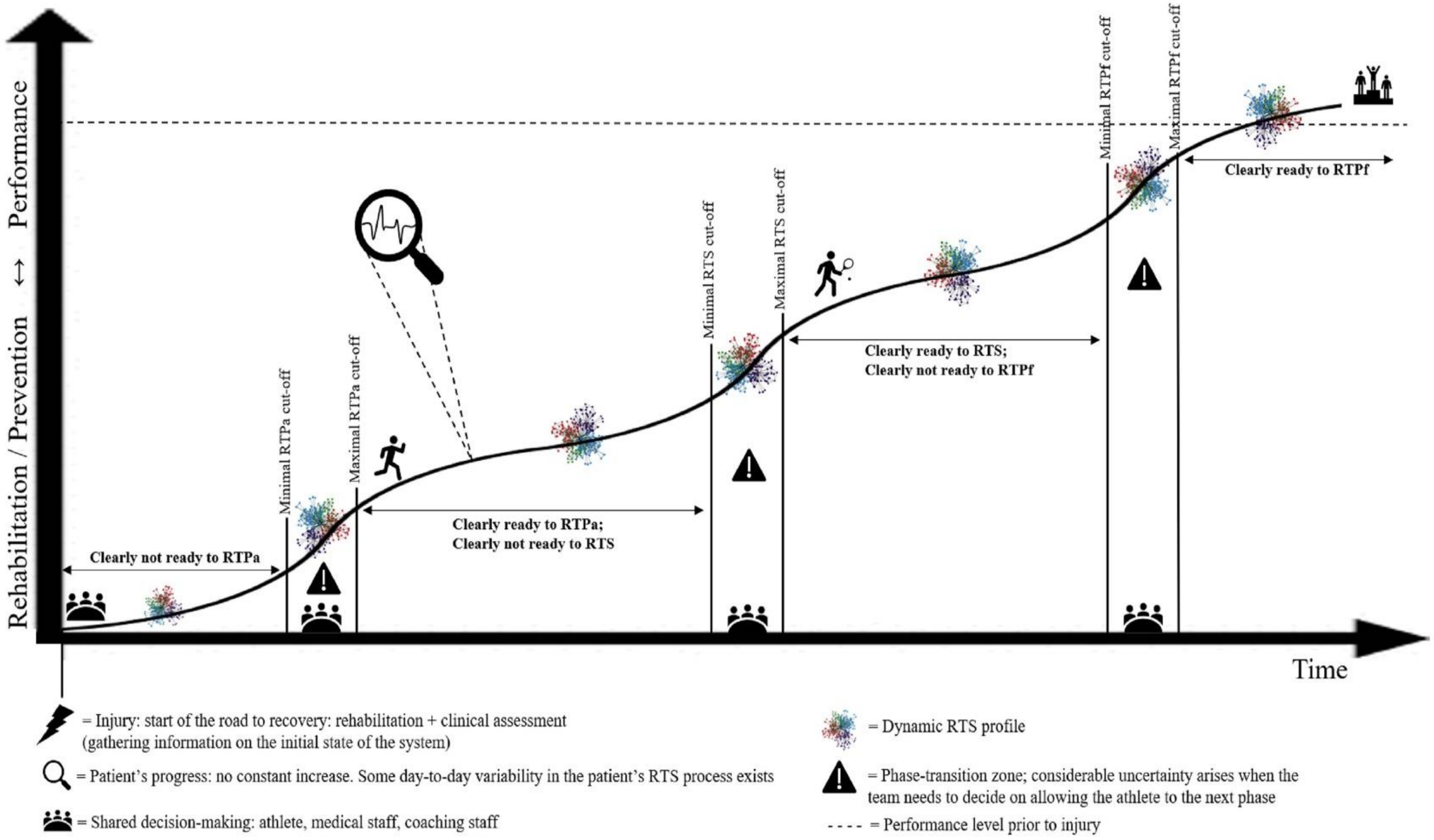

Figure 3 – Road to recovery along the RTS continuum. The x-axis denotes 'Time', and the y-axis denotes the constant field of tension between rehabilitation/prevention and performance along the RTS continuum. While RTPf is a nonlinear process, the figure above depicts a more or less ideal course. The progress curve emerges due to the dynamic RTS profile (see figure 2) over time. An example of the interpretation of minimal and maximal cut-offs for RTS decisions can be: athletes with a lower reinjury risk but who are less advanced in their rehabilitation can possibly progress earlier to the next phase, while athletes with a higher reinjury risk could benefit from making further progress in their rehabilitation before being allowed to the next phase. Furthermore, (elite) athletes can benefit from preinjury load monitoring, since this would yield additional information on the previous state of the system and help in determining goals for rehabilitation, prevention and training. RTPa = Return to participation; RTS = Return to sport; RTPf = Return to performance.

Directions for future research

Future research should explore substantiating and establishing a solid management pathway together with a dynamic criteria-based RTS decision-making paradigm along the RTS continuum with clear cut-off values and ranges for individuals recovering from acute LAS injury. We hope this review can guide researchers in selecting RTS criteria to investigate. This is a crucial first step that needs to be progressed with scientific research and supported by clinicians in the field. Prospective studies that use a criteria-based approach for the RTS decision-making process combined with adequate follow-up measures to determine the success rate of this RTS decision are needed to develop an evidence-informed management pathway following LAS injury. Also, defining "successful" RTS decisions along the RTS continuum is warranted in order to objectively measure success or failure. For example, a successful RTPf decision should not only be characterised by an athlete returning to his or her defined sport and performing at or above his or her pre-injury level, but also by the fact that the athlete does not incur a re-injury in the following months or years. This is especially important with injuries that have high recurrence rates, as is the case for acute LAS injury. These prospective, criteria-based study designs, defining successful RTPa, RTS and RTPf, are a crucial first step that needs to be initiated in scientific research to aid clinicians in the RTS decision-making process, as well as to aid researchers in developing evidence-informed guidelines and approaches in the RTS decision-making process after LAS injury.

Therefore, an international multidisciplinary enterprise has to be undertaken to connect both researchers and clinicians to the goal of bridging the gap between research and clinical practice and developing international consensus to select the best possible criteria that can be used throughout LAS injury management and decision-making processes. A modified Delphi process has been carried out for the clinical assessment following LAS injury and has already lead to some promising first results [156,208,209]. The Delphi process and corresponding consensus statements could form the first step to align practitioners and inspire researchers to develop and implement dynamic RTS clearance profiles that capture all relevant biopsychosocial aspects of a patient with a LAS injury. Inspiration for this continuing process can possibly be found in other domains, such as injury prevention and health promotion research (e.g. Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) model, Translating Research into Injury Prevention Practice (TRIPP) framework, six-stage operational framework for individualising injury risk management in sport) [210-213]. Using a knowledge transfer scheme to make the gap between science and practice smaller could provide valuable input for this ongoing process [214]. If these steps are successful, on field results can be evaluated through epidemiological research on reinjury rates, and short- and long-term cost effectiveness analyses can be undertaken.

Other areas that require further investigation are the clinical assessment, functional and sport-specific performance testing domains. It should be the objective of researchers to provide or advise relevant tests that can be performed clinically and which are able to identify the current progress of a patient or athlete through the RTS continuum after LAS injury. A good starting point would be to map the clinimetric characteristics (e.g. reliability, predictive values, specificity, likelihood ratios) of proposed tests. This could identify gaps within available tests and open the possibility for the development of new tests. Since humans can be considered as CAS, quantitative data will not always expose inefficiencies in movement patterns, as the system can look for alternative solutions to maintain performance (even though significant deficits could exist). Thus, tests assessing both quantitative performance data and movement quality should be integrated within the RTS decision-making continuum.

A more daunting challenge for future research is to determine how clinicians would most benefit from this complexity science paradigm and also how it would create high-quality and clinician friendly treatments and assessments based on the principles and concepts of CAS. The most important CAS within this framework is the patient. Future prospective studies should therefore include psychological, behavioural and social factors related to RTS in LAS and CAI patients in order to gain valuable insights into how these constraints interact with the progression of the patient along the rehabilitation and RTS continuum. These perspectives will help us to look beyond the injured joint and treat patients in a more holistic way.

While most of the sports medicine and sports science world is shifting its focus towards the exploration and utilisation of complexity science in research, major incentives for high-quality reductionist research have to keep being created (e.g. isolated factors, differences in isolated treatment strategies). This final comment is of great importance, as both paradigms reinforce each other and can symbiotically co-exist.

Limitations

The biggest limitation of this review is that no direct evidence was available regarding the prospective use of RTS tests and criteria. For this reason, a narrative synthesis was written based upon the findings of the search process of the systematic review. The RTS variables suggested in this review are a theoretical description based on empirical research that is linked to relevant tests in ankle rehabilitation throughout the RTS continuum. These variables need to be applied to actual RTS decisions within prospective research designs to evaluate their relevance. We realize that the perfect decision-making model with the perfect measurements and perfect criteria does not exist, due to the ubiquitous nature of complexity. However, this should not keep us from striving towards a best-care model and reminds us of the beauty of our work that combines rigorous science and the delicate art of guiding injured athletes back to their preinjury level and beyond. Awareness was also raised in the LAS and CAI literature to not oversimplify the multi-dimensional problems and consequences faced by LAS and CAI patients [209,215]. It was not our intention to provide a static framework, but to suggest possible rationales and considerations for a future dynamic criteria-based RTS decision-making paradigm. Hence, the principle of self-organization will automatically ensure that what is deemed useful or relevant is adopted by the (health care) system, and what seems implausible or too controversial is automatically ignored or rejected. This is an important consideration as the road from research to implementation is a rocky one and barriers to implementation need to be identified [216]. For example, will athletes, coaches, clubs, fans accept the criteria-based approach if it will take them longer to RTS, while currently a (very) fast RTS is possible even though a greater risk of reinjury and long term sequalae exist? With this paper, we aspired to stimulate the debate on RTS in LAS (and adjacent CAI) by fuelling critical thinking, contributing to the development process of a criteria-based decision-making approach in this population, and at best to inspire researchers, practitioners and students. Finally, Goodhart's law cautions that the more an evaluation of performance becomes an expectation, the poorer it becomes as a discriminator of individual performances. In other words: "*When a measure becomes a target, it ceases to be a good measure*" [217]. Therefore, we advocate for a sensible approach in establishing, implementing, and applying any criteria-based RTS decision-making paradigm in clinical practice and research. The goal should always be to assess whether athletes are truly ready to safely resume sports or not, instead of training them to pass the predetermined criteria without them being actually ready for RTS.

Conclusions

No studies were identified which used a criteria-based RTS decision-making process for patients with LAS injury. Therefore, we provided the reader with an overview of relevant retrieved questionnaires, clinical assessment measures, functional and sport-specific performance tests within ankle sprain populations and proposed RTS variables based upon empirical research throughout the RTS continuum. This narrative synthesis encompasses rationales and considerations for RTS decision-making following LAS injury. We advocate for the implementation of complex systems theory into the RTS decision-making paradigm and the utilisation of the RTS continuum by the 2016 Consensus statement on RTS [38]. In order to develop and implement a criteria-based and evidence-founded RTS clearance profile following LAS injury, these variables need to be applied to actual RTS decisions within future prospective research designs to evaluate their significance. The aims of future research should be to reach consensus on the "to-be-included" variables, the cut-offs and ranges of these variables that would serve as criteria, and to conduct rigorous scientific evaluation of these criteria. In short, it is time to develop a criteria-based RTS decision-making paradigm for acute LAS injury.

References

1. Doherty C, Delahunt E, Caulfield B, Hertel J, Ryan J, Bleakley C. The Incidence and Prevalence of Ankle Sprain Injury: A Systematic Review and Meta-Analysis of Prospective Epidemiological Studies. *Sports Medicine.* 2014;44(1):123-140.
2. Drakos MC, Domb B, Starkey C, Callahan L, Allen AA. Injury in the national basketball association: a 17-year overview. *Sports Health.* 2010;2(4):284-290.
3. Fong DTP, Hong YL, Chan LK, Yung PSH, Chan KM. A systematic review on ankle injury and ankle sprain in sports. *Sports Medicine.* 2007;37(1):73-94.
4. Jacobs CL, Hincapie CA, Cassidy JD. Musculoskeletal injuries and pain in dancers: a systematic review update. *J Dance Med Sci.* 2012;16(2):74-84.
5. Waterman BR, Owens BD, Davey S, Zacchilli MA, Belmont PJ. The Epidemiology of Ankle Sprains in the United States. *Journal of Bone and Joint Surgery-American Volume.* 2010;92A(13):2279-2284.
6. Wolfenden HEG, Angioi M. Musculoskeletal Injury Profile of Circus Artists A Systematic Review of the Literature. *Medical Problems of Performing Artists.* 2017;32(1):51-59.
7. Cumps E, Verhagen E, Meeusen R. Prospective epidemiological study of basketball injuries during one competitive season: Ankle sprains and overuse knee injuries. *Journal of Sports Science and Medicine.* 2007;6(2):204-211.
8. Beynnon BD, Murphy DF, Alosa DM. Predictive factors for lateral ankle sprains: A literature review. *Journal of Athletic Training.* 2002;37(4):376-380.
9. Bahr R, Bahr IA. Incidence of acute volleyball injuries: A prospective cohort study of injury mechanisms and risk factors. *Scandinavian Journal of Medicine & Science in Sports.* 1997;7(3):166-171.
10. Gribble PA, Bleakley CM, Caulfield BM, et al. Evidence review for the 2016 International Ankle Consortium consensus statement on the prevalence, impact and long-term consequences of lateral ankle sprains. *British Journal of Sports Medicine.* 2016;50(24):1496-+.
11. Swenson DM, Yard EE, Fields SK, Comstock RD. Patterns of Recurrent Injuries Among US High School Athletes, 2005-2008. *American Journal of Sports Medicine.* 2009;37(8):1586-1593.
12. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: Summary and recommendations for injury prevention initiatives. *Journal of Athletic Training.* 2007;42(2):311-319.
13. Malliaropoulos N, Ntessalen M, Papacostas E, Longo UG, Maffulli N. Reinjury After Acute Lateral Ankle Sprains in Elite Track and Field Athletes. *American Journal of Sports Medicine.* 2009;37(9):1755-1761.
14. Konradsen L, Bech L, Ehrenbjerg M, Nickelsen T. Seven years follow-up after ankle inversion trauma. *Scandinavian Journal of Medicine & Science in Sports.* 2002;12(3):129-135.
15. Delahunt E, Coughlan GF, Caulfield B, Nightingale EJ, Lin CWC, Hiller CE. Inclusion Criteria When Investigating Insufficiencies in Chronic Ankle Instability. *Medicine and Science in Sports and Exercise.* 2010;42(11):2106-2121.

16. Hertel J. Functional anatomy, pathomechanics, and pathophysiology of lateral ankle instability. *Journal of Athletic Training.* 2002;37(4):364-375.
17. Hiller CE, Kilbreath SL, Refshauge KM. Chronic Ankle Instability: Evolution of the Model. *Journal of Athletic Training.* 2011;46(2):133-141.
18. Harrington KD. Degenerative arthritis of the ankle secondary to long standing lateral ligament instability. *J Bone Joint Surg.* 1979;61A:354-361.
19. Landeros O, F rost HM, Higgins CC. Post traumatic anterior ankle instability. *Clin Orthop.* 1968;56:169-178.
20. Al-Mahrouqi MM, Macdonald DA, Vicenzino B, Smith MD. Physical Impairments in Adults With Ankle Osteoarthritis: A Systematic Review and Meta-analysis. *Journal of Orthopaedic & Sports Physical Therapy.* 2018;48(6):449-+.
21. Kerkhoffs GM, van den Bekerom M, Elders LAM, et al. Diagnosis, treatment and prevention of ankle sprains: an evidence-based clinical guideline. *British Journal of Sports Medicine.* 2012;46(12):854-860.
22. McKay GD, Goldie PA, Payne WR, Oakes BW. Ankle injuries in basketball: injury rate and risk factors. *British Journal of Sports Medicine.* 2001;35(2):103-108.
23. Birrer RB, Fani-Salek MH, Totten VY, Herman LM, Politi V. Managing ankle injuries in the emergency department. *Journal of Emergency Medicine.* 1999;17(4):651-660.
24. Gribble PA, Bleakley CM, Caulfield BM, et al. 2016 consensus statement of the International Ankle Consortium: prevalence, impact and long-term consequences of lateral ankle sprains. *British Journal of Sports Medicine.* 2016;50(24):1493-1495.
25. Feger MA, Glaviano NR, Donovan L, et al. Current Trends in the Management of Lateral Ankle Sprain in the United States. *Clinical Journal of Sport Medicine.* 2017;27(2):145-152.
26. Vuurberg G, Hoorntje A, Wink LM, et al. Diagnosis, treatment and prevention of ankle sprains: update of an evidence-based clinical guideline. *Br J Sports Med.* 2018.
27. van Rijn RM, van Ochten J, Luijsterburg PAJ, van Middelkoop M, Koes BW, Bierma-Zeinstra SMA. Effectiveness of additional supervised exercises compared with conventional treatment alone in patients with acute lateral ankle sprains: systematic review. *Bmj-British Medical Journal.* 2010;341:11.
28. Steib S, Zech A, Hentschke C, Pfeifer K. Fatigue-Induced Alterations of Static and Dynamic Postural Control in Athletes With a History of Ankle Sprain. *Journal of Athletic Training.* 2013;48(2):203-208.
29. Boyce SH, Quigley MA, Campbell S. Management of ankle sprains: a randomised controlled trial of the treatment of inversion injuries using an elastic support bandage or an Aircast ankle brace. *British Journal of Sports Medicine.* 2005;39(2):91-96.
30. McKay G, Goldie P, Payne WR, Oakes BW, Watson LF. A prospective study of injuries in basketball: A total profile and comparison by gender and standard of competition. *Journal of Science and Medicine in Sport.* 2001;4(2):196-211.

31. van der Wees PJ, Hendriks EJM, Jansen MJ, van Beers H, de Bie RA, Dekker J. Adherence to physiotherapy clinical guideline acute ankle injury and determinants of adherence: a cohort study. *Bmc Musculoskeletal Disorders.* 2007;8:7.
32. Dingenen B, Gokeler A. Optimization of the Return-to-Sport Paradigm After Anterior Cruciate Ligament Reconstruction: A Critical Step Back to Move Forward. *Sports Med.* 2017;47(8):1487-1500.
33. Rambaud AJM, Ardern CL, Thoreux P, Regnaux JP, Edouard P. Criteria for return to running after anterior cruciate ligament reconstruction: a scoping review. *Br J Sports Med.* 2018.
34. van der Horst N, van de Hoef S, Reurink G, Huisstede B, Backx F. Return to Play After Hamstring Injuries: A Qualitative Systematic Review of Definitions and Criteria. *Sports Med.* 2016;46(6):899-912.
35. Hickey JT, Timmins RG, Maniar N, Williams MD, Opar DA. Criteria for Progressing Rehabilitation and Determining Return-to-Play Clearance Following Hamstring Strain Injury: A Systematic Review. *Sports Med.* 2017;47(7):1375-1387.
36. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *Bmj.* 2015;350:g7647.
37. Tassignon B, Verschueren J, Smith MD, et al. *Return to play measurements and criteria after ankle sprains: a systematic review.* http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017060910: PROSPERO;2017.
38. Ardern CL, Glasgow P, Schneiders A, et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *British Journal of Sports Medicine.* 2016;50(14):853-864.
39. Gribble PA, Delahunt E, Bleakley C, et al. Selection Criteria for Patients With Chronic Ankle Instability in Controlled Research: A Position Statement of the International Ankle Consortium. *Journal of Orthopaedic & Sports Physical Therapy.* 2013;43(8):585-591.
40. Gribble PA, Delahunt E, Bleakley C, et al. Selection criteria for patients with chronic ankle instability in controlled research: a position statement of the International Ankle Consortium. *British Journal of Sports Medicine.* 2014;48(13):6.
41. Gribble PA, Delahunt E, Bleakley CM, et al. Selection Criteria for Patients With Chronic Ankle Instability in Controlled Research: A Position Statement of the International Ankle Consortium. *Journal of Athletic Training.* 2014;49(1):121-127.
42. Ouzzani M, Hammady H, Zbys Fedorowicz Z, Elmagarmid A. Rayyan - webb and mobile app for systematic reviews. *Systematic Reviews.* 2016;5:210.
43. Haywood KL, Hargreaves J, Lamb SE. Multi-item outcome measures for lateral ligament injury of the ankle: a structured review. *Journal of Evaluation in Clinical Practice.* 2004;10(2):339-352.
44. Donahue M, Simon J, Docherty CL. Critical review of self-reported functional ankle instability measures. *Foot Ankle Int.* 2011;32(12):1140-1146.

45. Simon J, Donahue M, Docherty CL. Critical review of self-reported functional ankle instability measures: a follow up. *Phys Ther Sport.* 2014;15(2):97-100.

46. Jia Y, Huang H, Gagnier JJ. A systematic review of measurement properties of patient-reported outcome measures for use in patients with foot or ankle diseases. *Qual Life Res.* 2017;26(8):1969-2010.

47. da Cunha RA, Hazime FA, da Silva Martins MC, Ferreira M, de Castro Pochini A, Ejnisman B. Translation, Cross-cultural Adaptation, and Clinimetric Testing of Instruments Used to Assess Patients With Ankle Sprain in the Brazilian Population. *J Orthop Sports Phys Ther.* 2016;46(12):1042-1050.

48. Anderson SJ. When to return to play after an ankle sprain. *Phys Sportsmed.* 2002;30(12):39.

49. Chamorro-Moriana G, Ridao-Fernandez C, Ojeda J, Benitez-Lugo M, Sevillano JL. Reliability and Validity Study of the Chamorro Assisted Gait Scale for People with Sprained Ankles, Walking with Forearm Crutches. *PLoS One.* 2016;11(5):e0155225.

50. Arnold BL, Wright CJ, Ross SE. Functional ankle instability and health-related quality of life. *J Athl Train.* 2011;46(6):634-641.

51. Houston MN, Hoch JM, Hoch MC. Patient-Reported Outcome Measures in Individuals With Chronic Ankle Instability: A Systematic Review. *Journal of Athletic Training.* 2015;50(10):1019-1033.

52. Perron M, Hebert LJ, McFadyen BJ, Belzile S, Regniere M. The ability of the Biodex Stability System to distinguish level of function in subjects with a second-degree ankle sprain. *Clin Rehabil.* 2007;21(1):73-81.

53. Repo JP, Tukiainen EJ, Roine RP, Ilves O, Jarvenpaa S, Hakkinen A. Reliability and validity of the Finnish version of the Lower Extremity Functional Scale (LEFS). *Disabil Rehabil.* 2017;39(12):1228-1234.

54. Larmer PJ, McNair PJ, Smythe L, Williams M. Ankle sprains: patient perceptions of function and performance of physical tasks. A mixed methods approach. *Disabil Rehabil.* 2011;33(23-24):2299-2304.

55. Williams GN, Molloy JM, DeBerardino TM, Arciero RA, Taylor DC. Evaluation of the Sports Ankle Rating System in young, athletic individuals with acute lateral ankle sprains. *Foot Ankle Int.* 2003;24(3):274-282.

56. Johnson MR, Stoneman PD. Comparison of a lateral hop test versus a forward hop test for functional evaluation of lateral ankle sprains. *J Foot Ankle Surg.* 2007;46(3):162-174.

57. Johanson NA, Liang MH, Daltroy L, Rudicel S, Richmond J. American Academy of Orthopaedic Surgeons lower limb outcomes assessment instruments. Reliability, validity, and sensitivity to change. *J Bone Joint Surg Am.* 2004;86-a(5):902-909.

58. Niki H, Tatsunami S, Haraguchi N, et al. Development of the patient-based outcome instrument for foot and ankle: part 2: results from the second field survey: validity of the Outcome Instrument for the foot and ankle version 2. *J Orthop Sci.* 2011;16(5):556-564.

59. Weel H, Zwiers R, Azim D, et al. Validity and reliability of a Dutch version of the Foot and Ankle Ability Measure. *Knee Surg Sports Traumatol Arthrosc.* 2016;24(4):1348-1354.

60. Clanton TO, Matheny LM, Jarvis HC, Jeronimus AB. Return to play in athletes following ankle injuries. *Sports Health.* 2012;4(6):471-474.

61. Best R, Rembitzki I, Petersen W. Return to sports after collateral ligament injury of the ankle. *Arthroskopie.* 2016;29(1):13 - 21.

62. Glazer DD. Development and preliminary validation of the Injury-Psychological Readiness to Return to Sport (I-PRRS) scale. *J Athl Train.* 2009;44(2):185-189.

63. Cresswell S, Hodge K. Coping skills: role of trait sport confidence and trait anxiety. *Percept Mot Skills.* 2004;98(2):433-438.

64. Vealey RS. Conceptualization of Sport-Confidence and Competitive Orientation: Preliminary Investigation and Instrument Development. *Journal of sport psychology.* 1986;8(3):221-246.

65. Gerber JP, Williams GN, Scoville CR, Arciero RA, Taylor DC. Persistent disability associated with ankle sprains: A prospective examination of an athletic population. *Foot & Ankle International.* 1998;19(10):653-660.

66. Baumbach SF, Fasser M, Polzer H, et al. Study protocol: the effect of whole body vibration on acute unilateral unstable lateral ankle sprain- a biphasic randomized controlled trial. *BMC Musculoskelet Disord.* 2013;14:22.

67. Bendahou M, Khiami F, Saidi K, et al. Compression stockings in ankle sprain: a multicenter randomized study. *Am J Emerg Med.* 2014;32(9):1005-1010.

68. Beynnon BD, Renstrom PA, Haugh L, Uh BS, Barker H. A prospective, randomized clinical investigation of the treatment of first-time ankle sprains. *Am J Sports Med.* 2006;34(9):1401-1412.

69. Gunay S, Karaduman A, Ozturk BB. Effects of Aircast brace and elastic bandage on physical performance of athletes after ankle injuries. *Acta Orthop Traumatol Turc.* 2014;48(1):10-16.

70. Hubbard TJ, Hicks-Little CA. Ankle ligament healing after an acute ankle sprain: an evidence-based approach. *J Athl Train.* 2008;43(5):523-529.

71. Hunt KJ, Hurwit D, Robell K, Gatewood C, Botser IB, Matheson G. Incidence and Epidemiology of Foot and Ankle Injuries in Elite Collegiate Athletes. *Am J Sports Med.* 2017;45(2):426-433.

72. Kerkhoffs GM, Rowe BH, Assendelft WJ, Kelly KD, Struijs PA, van Dijk CN. Immobilisation for acute ankle sprain. A systematic review. *Arch Orthop Trauma Surg.* 2001;121(8):462-471.

73. Kerkhoffs GM, Struijs PA, Marti RK, Assendelft WJ, Blankevoort L, van Dijk CN. Different functional treatment strategies for acute lateral ankle ligament injuries in adults. *Cochrane Database Syst Rev.* 2002(3):Cd002938.

74. Kerkhoffs GM, Rowe BH, Assendelft WJ, Kelly K, Struijs PA, van Dijk CN. Immobilisation and functional treatment for acute lateral ankle ligament injuries in adults. *Cochrane Database Syst Rev.* 2002(3):Cd003762.

75. Kerkhoffs GM, Handoll HH, de Bie R, Rowe BH, Struijs PA. Surgical versus conservative treatment for acute injuries of the lateral ligament complex of the ankle in adults. *Cochrane Database Syst Rev.* 2007(2):Cd000380.

76. Mendel FC, Dolan MG, Fish DR, Marzo J, Wilding GE. Effect of high-voltage pulsed current on recovery after grades I and II lateral ankle sprains. *J Sport Rehabil.* 2010;19(4):399-410.

77. Petrella RJ, Petrella MJ, Cogliano A. Periarticular hyaluronic acid in acute ankle sprain. *Clin J Sport Med.* 2007;17(4):251-257.

78. Wilson RW, Gansneder BM. Measures of functional limitation as predictors of disablement in athletes with acute ankle sprains. *J Orthop Sports Phys Ther.* 2000;30(9):528-535.

79. Verhagen E, van Tulder M, van der Beek AJ, Bouter LM, van Mechelen W. An economic evaluation of a proprioceptive balance board training programme for the prevention of ankle sprains in volleyball. *British Journal of Sports Medicine.* 2005;39(2):111-115.

80. McCann RS, Kosik KB, Terada M, Beard MQ, Buskirk GE, Gribble PA. Acute lateral ankle sprain prediction in collegiate women's soccer players. *Int J Sports Phys Ther.* 2018;13(1):12-18.

81. Gokeler A, Welling W, Zaffagnini S, Seil R, Padua D. Development of a test battery to enhance safe return to sports after anterior cruciate ligament reconstruction. *Knee Surgery Sports Traumatology Arthroscopy.* 2017;25(1):192-199.

82. Grindem H, Snyder-Mackler L, Moksnes H, Engebretsen L, Risberg MA. Simple decision rules can reduce reinjury risk by 84% after ACL reconstruction: the Delaware-Oslo ACL cohort study. *Br J Sports Med.* 2016;50(13):804-808.

83. Herbst E, Hoser C, Hildebrandt C, et al. Functional assessments for decision-making regarding return to sports following ACL reconstruction. Part II: clinical application of a new test battery. *Knee Surgery Sports Traumatology Arthroscopy.* 2015;23(5):1283-1291.

84. Kyritsis P, Bahr R, Landreau P, Miladi R, Witvrouw E. Likelihood of ACL graft rupture: not meeting six clinical discharge criteria before return to sport is associated with a four times greater risk of rupture. *Br J Sports Med.* 2016;50(15):946-951.

85. Rambaud AJM, Semay B, Samozino P, et al. Criteria for Return to Sport after Anterior Cruciate Ligament reconstruction with lower reinjury risk (CR'STAL study): protocol for a prospective observational study in France. *BMJ Open.* 2017;7(6):e015087.

86. Mendiguchia J, Martinez-Ruiz E, Edouard P, et al. A Multifactorial, Criteria-based Progressive Algorithm for Hamstring Injury Treatment. *Med Sci Sports Exerc.* 2017;49(7):1482-1492.

87. Shrier I, Serner A, Wangensteen A, Steele RJ, Weir A. Measuring heterogeneity of reinjury risk assessments at the time of clearance to return to play: A feasibility study. *J Sci Med Sport.* 2017;20(3):255-260.

88. van der Horst N, Backx F, Goedhart EA, Huisstede BM. Return to play after hamstring injuries in football (soccer): a worldwide Delphi procedure regarding definition, medical criteria and decision-making. *Br J Sports Med.* 2017;51(22):1583-1591.

89. Zambaldi M, Beasley I, Rushton A. Return to play criteria after hamstring muscle injury in professional football: a Delphi consensus study. *Br J Sports Med.* 2017;51(16):1221-1226.

90. Bekker S, Clark AM. Bringing complexity to sports injury prevention research: from simplification to explanation. In: *Br J Sports Med.* Vol 50. England2016:1489-1490.

91. Cook C. Predicting future physical injury in sports: it's a complicated dynamic system. In: *Br J Sports Med.* Vol 50. England2016:1356-1357.

92. Glazier PS. Towards a Grand Unified Theory of sports performance. *Hum Mov Sci.* 2017;56(Pt A):139-156.

93. Gokeler A, Verhagen E, Hirschmann MT. Let us rethink research for ACL injuries: a call for a more complex scientific approach. In: *Knee Surg Sports Traumatol Arthrosc.* Vol 26. Germany2018:1303-1304.

94. Harbourne RT, Stergiou N. Movement variability and the use of nonlinear tools: principles to guide physical therapist practice. *Phys Ther.* 2009;89(3):267-282.

95. Hulme A, Finch CF. From monocausality to systems thinking: a complementary and alternative conceptual approach for better understanding the development and prevention of sports injury. *Inj Epidemiol.* 2015;2(1):31.

96. Stergiou N, Decker LM. Human movement variability, nonlinear dynamics, and pathology: is there a connection? *Hum Mov Sci.* 2011;30(5):869-888.

97. Sturmberg JP, Martin CM, Katerndahl DA. Systems and complexity thinking in the general practice literature: an integrative, historical narrative review. *Ann Fam Med.* 2014;12(1):66-74.

98. Vaz DV, Silva PL, Mancini MC, Carello C, Kinsella-Shaw J. Towards an ecologically grounded functional practice in rehabilitation. *Hum Mov Sci.* 2017;52:117-132.

99. Balague N, Torrents C, Hristovski R, Kelso JA. Sport science integration: An evolutionary synthesis. *Eur J Sport Sci.* 2017;17(1):51-62.

100. Pol R, Hristovski R, Medina D, Balague N. From microscopic to macroscopic sports injuries. Applying the complex dynamic systems approach to sports medicine: a narrative review. *Br J Sports Med.* 2018.

101. Bahr R. Why screening tests to predict injury do not work-and probably never will...: a critical review. *Br J Sports Med.* 2016;50(13):776-780.

102. Verhagen E, van Dyk N, Clark N, Shrier I. Do not throw the baby out with the bathwater; screening can identify meaningful risk factors for sports injuries. *Br J Sports Med.* 2018.

103. Adams D. *The Salmon of Doubt: Hitchhiking the Galaxy One Last Time.* United Kingdom: William Heinemann Ltd.; 2002.

104. Bittencourt NF, Meeuwisse WH, Mendonca LD, Nettel-Aguirre A, Ocarino JM, Fonseca ST. Complex systems approach for sports injuries: moving from risk factor identification to injury pattern recognition-narrative review and new concept. *Br J Sports Med.* 2016.

105. Wikstrom EA, Hubbard-Turner T, McKeon PO. Understanding and treating lateral ankle sprains and their consequences: a constraints-based approach. *Sports Med.* 2013;43(6):385-393.

106. Briet JP, Houwert RM, Hageman M, Hietbrink F, Ring DC, Verleisdonk E. Factors associated with pain intensity and physical limitations after lateral ankle sprains. *Injury.* 2016;47(11):2565-2569.

107. Brown CN, Padua DA, Marshall SW, Guskiewicz KM. Variability of motion in individuals with mechanical or functional ankle instability during a stop jump maneuver. *Clin Biomech (Bristol, Avon).* 2009;24(9):762-768.

108. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Balance failure in single limb stance due to ankle sprain injury: an analysis of center of pressure using the fractal dimension method. *Gait Posture.* 2014;40(1):172-176.

109. Doherty C, Bleakley C, Hertel J, et al. Inter-joint coordination strategies during unilateral stance 6-months following first-time lateral ankle sprain. *Clin Biomech (Bristol, Avon).* 2015;30(2):129-135.

110. Doherty C, Bleakley CM, Hertel J, Caulfield B, Ryan J, Delahunt E. Laboratory Measures of Postural Control During the Star Excursion Balance Test After Acute First-Time Lateral Ankle Sprain. *J Athl Train.* 2015;50(6):651-664.

111. Brown C, Bowser B, Simpson KJ. Movement variability during single leg jump landings in individuals with and without chronic ankle instability. *Clin Biomech (Bristol, Avon).* 2012;27(1):52-63.

112. Doherty C, Bleakley C, Hertel J, et al. Lower Limb Interjoint Postural Coordination One Year after First-Time Lateral Ankle Sprain. *Med Sci Sports Exerc.* 2015;47(11):2398-2405.

113. Koldenhoven RM, Feger MA, Fraser JJ, Hertel J. Variability in center of pressure position and muscle activation during walking with chronic ankle instability. *J Electromyogr Kinesiol.* 2018;38:155-161.

114. Terada M, Bowker S, Thomas AC, et al. Alterations in stride-to-stride variability during walking in individuals with chronic ankle instability. *Hum Mov Sci.* 2015;40:154-162.

115. McGrath D, Patterson M, Persson UM, Caulfield B. Frontal-Plane Variability in Foot Orientation During Fatiguing Running Exercise in Individuals With Chronic Ankle Instability. *J Athl Train.* 2017;52(11):1019-1027.

116. Shrier I, Safai P, Charland L. Return to play following injury: whose decision should it be? *Br J Sports Med.* 2014;48(5):394-401.

117. Safran MR, Benedetti RS, Bartozolli AR, Mandelbaum BR. Lateral ankle sprains: a comprehensive review. Part 1: etiology, pathoanatomy, histopathogenesis, and diagnosis. *Medicine and Science in Sports and Exercise.* 1999;31(7 Suppl):S429–437.

118. O'Donoghue DH. *Treatment of Injuries to Athletes.* Philadelphia: W. B. Saunders; 1976.

119. Thorndike A. *Athletic Injuries: Prevention, Diagnosis and Treatment.* Philadelphia: Lea and Febiger; 1962.

120. Garrick JG. The frequency of injury, mechanism of injury, and epidemiology of ankle sprains. *American Journal of Sports Medicine.* 1977;5:241-242.

121. O'Donoghue DH. *Treatment of ankle injuries.* Vol 57: Northwest Med.; 1958.

122. Iversen LD, Clawson DK. *Manual of Acute Orthopaedics.* Boston: Little, Brown, and Company; 1982.

123. Medina McKeon JM, Bush HM, Reed A, Whittington A, Uhl TL, McKeon PO. Return-to-play probabilities following new versus recurrent ankle sprains in high school athletes. *J Sci Med Sport.* 2014;17(1):23-28.

124. McCann R, Kosik K, Terada M, Gribble P. Residual Impairments and Activity Limitations at Return to Play from a Lateral Ankle Sprain. *International Journal of Athletic Therapy & Training.* 2018;23(2):83-88.

125. Kobayashi T, Yoshida M, Gamada K. Intrinsic Predictive Factors of Noncontact Lateral Ankle Sprain in Collegiate Athletes: A Case-Control Study. *Orthop J Sports Med.* 2013;1(7):2325967113518163.

126. de Noronha M, Refshauge KM, Herbert RD, Kilbreath SL, Hertel J. Do voluntary strength, proprioception, range of motion, or postural sway predict occurrence of lateral ankle sprain? *Br J Sports Med.* 2006;40(10):824-828; discussion 828.

127. Pope R, Herbert R, Kirwan J. Effects of ankle dorsiflexion range and pre-exercise calf muscle stretching on injury risk in Army recruits. *Aust J Physiother.* 1998;44(3):165-172.

128. Tropp H, Ekstrand J, Gillquist J. Stabilometry in functional instability of the ankle and its value in predicting injury. *Med Sci Sports Exerc.* 1984;16(1):64-66.

129. Watson AW. Ankle sprains in players of the field-games Gaelic football and hurling. *J Sports Med Phys Fitness.* 1999;39(1):66-70.

130. McGuine TA, Keene JS. The effect of a balance training program on the risk of ankle sprains in high school athletes. *Am J Sports Med.* 2006;34(7):1103-1111.

131. Wang HK, Chen CH, Shiang TY, Jan MH, Lin KH. Risk-factor analysis of high school basketball-player ankle injuries: a prospective controlled cohort study evaluating postural sway, ankle strength, and flexibility. *Arch Phys Med Rehabil.* 2006;87(6):821-825.

132. de Noronha M, Franca LC, Haupenthal A, Nunes GS. Intrinsic predictive factors for ankle sprain in active university students: a prospective study. *Scand J Med Sci Sports.* 2013;23(5):541-547.

133. Hrysomallis C, McLaughlin P, Goodman C. Balance and injury in elite Australian footballers. *Int J Sports Med.* 2007;28(10):844-847.

134. Kobayashi T, Tanaka M, Shida M. Intrinsic Risk Factors of Lateral Ankle Sprain: A Systematic Review and Meta-analysis. *Sports Health.* 2016;8(2):190-193.

135. Willems TM, Witvrouw E, Delbaere K, Mahieu N, De Bourdeaudhuij I, De Clercq D. Intrinsic risk factors for inversion ankle sprains in male subjects: a prospective study. *Am J Sports Med.* 2005;33(3):415-423.

136. Trojian TH, McKeag DB. Single leg balance test to identify risk of ankle sprains. *Br J Sports Med.* 2006;40(7):610-613; discussion 613.

137. Rice H, Nunns M, House C, Fallowfield J, Allsopp A, Dixon S. High medial plantar pressures during barefoot running are associated with increased risk of ankle inversion injury in Royal Marine recruits. *Gait Posture.* 2013;38(4):614-618.

138. Hagen M, Asholt J, Lemke M, Lahner M. The angle-torque-relationship of the subtalar pronators and supinators in male athletes: A comparative study of soccer and handball players. *Technol Health Care.* 2016;24(3):391-399.

139. Verhagen EA, Van der Beek AJ, Bouter LM, Bahr RM, Van Mechelen W. A one season prospective cohort study of volleyball injuries. *Br J Sports Med.* 2004;38(4):477-481.

140. Kofotolis ND, Kellis E, Vlachopoulos SP. Ankle sprain injuries and risk factors in amateur soccer players during a 2-year period. *Am J Sports Med.* 2007;35(3):458-466.

141. Kofotolis N, Kellis E. Ankle sprain injuries: a 2-year prospective cohort study in female Greek professional basketball players. *J Athl Train.* 2007;42(3):388-394.

142. Panagiotakis E, Mok KM, Fong DT, Bull AMJ. Biomechanical analysis of ankle ligamentous sprain injury cases from televised basketball games: Understanding when, how and why ligament failure occurs. *J Sci Med Sport.* 2017;20(12):1057-1061.

143. Ekstrand J, Timpka T, Hagglund M. Risk of injury in elite football played on artificial turf versus natural grass: a prospective two-cohort study. *Br J Sports Med.* 2006;40(12):975-980.

144. Hershman EB, Anderson R, Bergfeld JA, et al. An analysis of specific lower extremity injury rates on grass and FieldTurf playing surfaces in National Football League Games: 2000-2009 seasons. *Am J Sports Med.* 2012;40(10):2200-2205.

145. Orchard JW, Powell JW. Risk of knee and ankle sprains under various weather conditions in American football. *Med Sci Sports Exerc.* 2003;35(7):1118-1123.

146. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Recovery From a First-Time Lateral Ankle Sprain and the Predictors of Chronic Ankle Instability: A Prospective Cohort Analysis. *Am J Sports Med.* 2016;44(4):995-1003.

147. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Dynamic Balance Deficits 6 Months Following First-Time Acute Lateral Ankle Sprain: A Laboratory Analysis. *J Orthop Sports Phys Ther.* 2015;45(8):626-633.

148. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Single-leg drop landing movement strategies in participants with chronic ankle instability compared with lateral ankle sprain 'copers'. *Knee Surg Sports Traumatol Arthrosc.* 2016;24(4):1049-1059.

149. Hubbard TJ. Ligament laxity following inversion injury with and without chronic ankle instability. *Foot Ankle Int.* 2008;29(3):305-311.

150. Hubbard TJ, Cordova M. Mechanical instability after an acute lateral ankle sprain. *Arch Phys Med Rehabil.* 2009;90(7):1142-1146.

151. Hubbard TJ, Wikstrom EA. Ankle sprain: pathophysiology, predisposing factors, and management strategies. *Open Access J Sports Med.* 2010;1:115-122.

152. Brostroem L. Sprained ankles. I. Anatomic lesions in recent sprains. *Acta Chir Scand.* 1964;128:483-495.

153. Chamberlain CS, Crowley E, Vanderby R. The spatio-temporal dynamics of ligament healing. *Wound Repair and Regeneration.* 2009;17(2):206-215.

154. Denegar CR, Hertel J, Fonseca J. The effect of lateral ankle sprain on dorsiflexion range of motion, posterior talar glide, and joint laxity. *J Orthop Sports Phys Ther.* 2002;32(4):166-173.

155. Schneiders A, Karas S. The accuracy of clinical tests in diagnosing ankle ligament injury. *European Journal of Physiotherapy.* 2016;18(4):245-253.

156. Delahunt E, Bleakley CM, Bossard DS, et al. Clinical assessment of acute lateral ankle sprain injuries (ROAST): 2019 consensus statement and recommendations of the International Ankle Consortium. *Br J Sports Med.* 2018.

157. Karlsson J, Eriksson BI, Renstrom PA. Subtalar ankle instability - A review. *Sports Medicine.* 1997;24(5):339-348.

158. Beynnon BD, Renstrom PA, Alosa DM, Baumhauer JF, Vacek PM. Ankle ligament injury risk factors: a prospective study of college athletes. *Journal of Orthopaedic Research.* 2001;19(2):213-220.

159. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Clinical Tests Have Limited Predictive Value for Chronic Ankle Instability When Conducted in the Acute Phase of a First-Time Lateral Ankle Sprain Injury. *Arch Phys Med Rehabil.* 2018;99(4):720-725.e721.

160. Hegedus EJ, McDonough S, Bleakley C, et al. Physical performance tests predict injury in National Collegiate Athletic Association athletes: a three-season prospective cohort study. *Br J Sports Med.* 2016.

161. Hegedus EJ, McDonough SM, Bleakley C, Baxter D, Cook CE. Clinician-friendly lower extremity physical performance tests in athletes: a systematic review of measurement properties and correlation with injury. Part 2-the tests for the hip, thigh, foot and ankle including the star excursion balance test. *British Journal of Sports Medicine.* 2015;49(10).

162. Gomez-Piqueras P, Gonzalez-Rubio J, Sainz de Baranda P, Najera A. Use of functional performance tests in sports: Evaluation proposal for football players in the rehabilitation phase. *Turk J Phys Med Rehab.* 2018;64(2):148-154.

163. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Dynamic balance deficits in individuals with chronic ankle instability compared to ankle sprain copers 1 year after a first-time lateral ankle sprain injury. *Knee Surg Sports Traumatol Arthrosc.* 2016;24(4):1086-1095.

164. Eechaute C, Vaes P, Duquet W. The dynamic postural control is impaired in patients with chronic ankle instability: reliability and validity of the multiple hop test. *Clin J Sport Med.* 2009;19(2):107-114.

165. Buchanan AS, Docherty CL, Schrader J. Functional performance testing in participants with functional ankle instability and in a healthy control group. *J Athl Train.* 2008;43(4):342-346.

166. Docherty CL, Valovich McLeod TC, Shultz SJ. Postural control deficits in participants with functional ankle instability as measured by the balance error scoring system. *Clin J Sport Med.* 2006;16(3):203-208.

167. Hiller CE, Refshauge KM, Herbert RD, Kilbreath SL. Balance and recovery from a perturbation are impaired in people with functional ankle instability. *Clin J Sport Med.* 2007;17(4):269-275.

168. Pourkazemi F, Hiller CE, Raymond J, Black D, Nightingale EJ, Refshauge KM. Predictors of recurrent sprains after an index lateral ankle sprain: a longitudinal study. *Physiotherapy.* 2017.

169. Terrier R, Degache F, Fourchet F, Gojanovic B, Forestier N. Assessment of evertor weakness in patients with chronic ankle instability: Functional versus isokinetic testing. *Clin Biomech (Bristol, Avon).* 2017;41:54-59.

170. Caffrey E, Docherty CL, Schrader J, Klossner J. The ability of 4 single-limb hopping tests to detect functional performance deficits in individuals with functional ankle instability. *J Orthop Sports Phys Ther.* 2009;39(11):799-806.

171. Dallinga JM, van der Does HT, Benjaminse A, Lemmink KA. Dynamic postural stability differences between male and female players with and without ankle sprain. *Phys Ther Sport.* 2016;17:69-75.

172. Ward S, Pearce AJ, Pietrosimone B, Bennell K, Clark R, Bryant AL. Neuromuscular deficits after peripheral joint injury: a neurophysiological hypothesis. *Muscle Nerve.* 2015;51(3):327-332.

173. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Postural control strategies during single limb stance following acute lateral ankle sprain. *Clin Biomech (Bristol, Avon).* 2014;29(6):643-649.

174. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Lower extremity function during gait in participants with first time acute lateral ankle sprain compared to controls. *J Electromyogr Kinesiol.* 2015;25(1):182-192.

175. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Single-leg drop landing motor control strategies following acute ankle sprain injury. *Scand J Med Sci Sports.* 2015;25(4):525-533.

176. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Single-leg drop landing movement strategies 6 months following first-time acute lateral ankle sprain injury. *Scand J Med Sci Sports.* 2015;25(6):806-817.

177. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Gait Biomechanics in Participants, Six Months after First-time Lateral Ankle Sprain. *Int J Sports Med.* 2016;37(7):577-583.

178. Doherty C, Bleakley C, Hertel J, et al. Coordination and Symmetry Patterns During the Drop Vertical Jump in People With Chronic Ankle Instability and Lateral Ankle Sprain Copers. *Phys Ther.* 2016;96(8):1152-1161.

179. Doherty C, Bleakley C, Hertel J, Caulfield B, Ryan J, Delahunt E. Locomotive biomechanics in persons with chronic ankle instability and lateral ankle sprain copers. *J Sci Med Sport.* 2016;19(7):524-530.

180. Eechaute C, De Ridder R, Maes T, et al. Evidence of a different landing strategy in subjects with chronic ankle instability. *Gait Posture.* 2017;52:62-67.

181. Doherty C, Bleakley C, Hertel J, et al. Coordination and symmetry patterns during the drop vertical jump, 6-months after first-time lateral ankle sprain. *J Orthop Res.* 2015;33(10):1537-1544.

182. Brown C, Padua D, Marshall SW, Guskiewicz K. Individuals with mechanical ankle instability exhibit different motion patterns than those with functional ankle instability and ankle sprain copers. *Clin Biomech (Bristol, Avon).* 2008;23(6):822-831.

183. Rosen A, Swanik C, Thomas S, Glutting J, Knight C, Kaminski TW. Differences in lateral drop jumps from an unknown height among individuals with functional ankle instability. *J Athl Train.* 2013;48(6):773-781.

184. Springer S, Gottlieb U. Effects of dual-task and walking speed on gait variability in people with chronic ankle instability: a cross-sectional study. *BMC Musculoskelet Disord.* 2017;18(1):316.

185. Benjaminse A, Otten B, Gokeler A, Diercks RL, Lemmink K. Motor learning strategies in basketball players and its implications for ACL injury prevention: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc.* 2017;25(8):2365-2376.

186. Gokeler A, Benjaminse A, Welling W, Alferink M, Eppinga P, Otten B. The effects of attentional focus on jump performance and knee joint kinematics in patients after ACL reconstruction. *Phys Ther Sport.* 2015;16(2):114-120.

187. Orth D, van der Kamp J, Memmert D, Savelsbergh GJP. Creative Motor Actions As Emerging from Movement Variability. *Front Psychol.* 2017;8:1903.

188. Renshaw I, Chow JY, Keith Davids K, Hammond J. A constraints-led perspective to understanding skill acquisition and game play: a basis for integration of motor learning theory and physical education praxis? *Physical Education and Sport Pedagogy.* 2010;15(2):117-137.

189. Schollhorn WI, Beckmann H, Davids K. Exploiting system fluctuations. Differential training in physical prevention and rehabilitation programs for health and exercise. *Medicina (Kaunas).* 2010;46(6):365-373.

190. Wulf G, Lewthwaite R. Optimizing performance through intrinsic motivation and attention for learning: The OPTIMAL theory of motor learning. *Psychon Bull Rev.* 2016;23(5):1382-1414.

191. Knicker AJ, Renshaw I, Oldham ARH, Cairns SP. Interactive Processes Link the Multiple Symptoms of Fatigue in Sport Competition. *Sports Medicine.* 2011;41(4):307-328.

192. Van Cutsem J, Marcora S, De Pauw K, Bailey S, Meeusen R, Roelands B. The Effects of Mental Fatigue on Physical Performance: A Systematic Review. *Sports Medicine.* 2017;47(8):1569-1588.

193. Taylor JL, Amann M, Duchateau J, Meeusen R, Rice CL. Neural contributions to muscle fatigue: from the brain to the muscle and back again. *Med Sci Sports Exerc.* 2016;48(11):2294-2306.

194. Coutinho D, Goncalves B, Wong DP, Travassos B, Coutts AJ, Sampaio J. Exploring the effects of mental and muscular fatigue in soccer players' performance. *Hum Mov Sci.* 2018;58:287-296.

195. Le Mansec Y, Pageaux B, Nordez A, Dorel S, Jubeau M. Mental fatigue alters the speed and the accuracy of the ball in table tennis. *J Sports Sci.* 2017:1-9.

196. Soligard T, Schwellnus M, Alonso JM, et al. How much is too much? (Part 1) International Olympic Committee consensus statement on load in sport and risk of injury. *Br J Sports Med.* 2016;50(17):1030-1041.

197. Schwellnus M, Soligard T, Alonso JM, et al. How much is too much? (Part 2) International Olympic Committee consensus statement on load in sport and risk of illness. *Br J Sports Med.* 2016;50(17):1043-1052.

198. Gabbett TJ. The training-injury prevention paradox: should athletes be training smarter and harder? *Br J Sports Med.* 2016;50(5):273-280.

199. Windt J, Gabbett TJ. How do training and competition workloads relate to injury? The workload-injury aetiology model. *Br J Sports Med.* 2017;51(5):428-435.

200. Blanch P, Gabbett TJ. Has the athlete trained enough to return to play safely? The acute:chronic workload ratio permits clinicians to quantify a player's risk of subsequent injury. *Br J Sports Med.* 2016;50(8):471-475.

201. Ardern CL, Osterberg A, Tagesson S, Gauffin H, Webster KE, Kvist J. The impact of psychological readiness to return to sport and recreational activities after anterior cruciate ligament reconstruction. *Br J Sports Med.* 2014;48(22):1613-1619.

202. Bauer M, Feeley BT, Wawrzyniak JR, Pinkowsky G, Gallo RA. Factors affecting return to play after anterior cruciate ligament reconstruction: a review of the current literature. *Phys Sportsmed.* 2014;42(4):71-79.

203. Christino MA, Fantry AJ, Vopat BG. Psychological Aspects of Recovery Following Anterior Cruciate Ligament Reconstruction. *J Am Acad Orthop Surg.* 2015;23(8):501-509.

204. Podlog L, Heil J, Schulte S. Psychosocial factors in sports injury rehabilitation and return to play. *Phys Med Rehabil Clin N Am.* 2014;25(4):915-930.

205. Laux P, Krumm B, Diers M, Flor H. Recovery-stress balance and injury risk in professional football players: a prospective study. *Journal of Sports Sciences.* 2015;33(20):2140-2148.

206. Milewski MD, Skaggs DL, Bishop GA, et al. Chronic Lack of Sleep is Associated With Increased Sports Injuries in Adolescent Athletes. *Journal of Pediatric Orthopaedics.* 2014;34(2):129-133.

207. Brehmer B. Dynamic decision making: human control of complex systems. *Acta Psychol (Amst).* 1992;81(3):211-241.

208. Bossard DS, Remus A, Doherty C, Gribble PA, Delahunt E. Developing consensus on clinical assessment of acute lateral ankle sprain injuries: protocol for an international and multidisciplinary modified Delphi process. *Br J Sports Med.* 2018.

209. Delahunt E, Gribble PA. Structured clinical assessment: a brake to stop the ankle joint 'rolling'. *Br J Sports Med.* 2018.

210. Finch C. A new framework for research leading to sports injury prevention. *J Sci Med Sport.* 2006;9(1-2):3-9; discussion 10.

211. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *Am J Public Health.* 1999;89(9):1322-1327.

212. Roe M, Malone S, Blake C, et al. A six stage operational framework for individualising injury risk management in sport. In: *Inj Epidemiol.* Vol 4. Germany2017:26.

213. van Mechelen W, Hlobil H, Kemper HC. Incidence, severity, aetiology and prevention of sports injuries. A review of concepts. *Sports Med.* 1992;14(2):82-99.

214. Verhagen E, Voogt N, Bruinsma A, Finch CF. A knowledge transfer scheme to bridge the gap between science and practice: an integration of existing research frameworks into a tool for practice. *British Journal of Sports Medicine.* 2014;48(8):698-701.

215. van Dijk CN, Vuurberg G. There is no such thing as a simple ankle sprain: clinical commentary on the 2016 International Ankle Consortium position statement. In: *Br J Sports Med.* Vol 51. England2017:485-486.

216. O'Brien J, Hägglund M, Bizzini M. Implementing injury prevention – the rocky road from rct to realworld injury reduction. *ASPETAR Sports Medicine Journal.* 2018;7(16):70-76.

217. Strathern M. 'Improving ratings': audit in the British University system. *European Review.* 1997;5(3):305-321.

Electronic Supplementary Material Table S1. Search strategies for all databases

Database	***Keywords***
PubMed	("Ankle Injuries"[Mesh] OR "ankle injury" OR "ankle sprain" OR "lateral ankle sprain" OR "ankle inversion trauma") AND (test OR "functional test" OR "functional tests" OR "functional testing" OR "static test" OR "mechanical test" OR "clinical test" OR "measurement" OR "criteria") AND ("Return to sport"[MeSH] OR "Reproducibility of results"[MeSH] OR "Sensitivity and Specificity"[MeSH] OR "Limit of detection"[MeSH] OR "return to sports" OR "return to play" OR "return to participation" OR "return to action" OR "return to sporting activities" OR "return to activity" OR "return to competition" OR "return to training" OR "sports participation" OR "return to performance" OR "return to level" OR "match fitness" OR "training fitness" OR "full fitness" OR "repetitive injury" OR "recurrent injury" OR "reinjury risk" OR "reinjury" OR "reinjury rate" OR "re-injury" OR "re-injury rate" OR validity OR reliability OR specificity OR sensitivity OR "repetitive sprain" OR "recurrent sprain")
Web of Science	("Ankle Injuries" OR "ankle injury" OR "ankle sprain" OR "lateral ankle sprain" OR "ankle inversion trauma") **AND** (test OR "functional test" OR "functional tests" OR "functional testing" OR "static test" OR "mechanical test" OR "clinical test" OR "measurement" OR "criteria") **AND** ("Return to sport" OR "Reproducibility of results" OR "Limit of detection" OR "return to sports" OR "return to play" OR "return to participation" OR "return to action" OR "return to sporting activities" OR "return to activity" OR "return to competition" OR "return to training" OR "sports participation" OR "return to performance" OR "return to level" OR "match fitness" OR "training fitness" OR "full fitness" OR "repetitive injury" OR "recurrent injury" OR "reinjury risk" OR "reinjury" OR "reinjury rate" OR "re-injury" OR "re-injury rate" OR validity OR reliability OR specificity OR sensitivity OR "repetitive sprain" OR "recurrent sprain")
PEDro	Ankle **AND** return
Scopus	TITLE-ABS-KEY (("ankle injuries" OR "ankle sprain" OR "ankle inversion trauma") **AND** (test OR measurement OR criteria) **AND** ("return to sport" OR fitness OR play OR reinjury OR re-injury OR validity OR reliability OR sensitivity OR specificity OR "recurrent sprain")) AND DOCTYPE (ar OR re)
Cochrane Library	("Ankle Injuries" OR "ankle injury" OR "ankle sprain" OR "lateral ankle sprain" OR "ankle inversion trauma") **AND** (test OR "functional test" OR "functional tests" OR "functional testing" OR "static test" OR "mechanical test" OR "clinical test" OR "measurement" OR "criteria") **AND** ("Return to sport" OR "Reproducibility of results" OR "Limit of detection" OR "return to sports" OR "return to play" OR "return to participation" OR "return to action" OR "return to sporting activities" OR "return to activity" OR "return to competition" OR "return to training" OR "sports participation" OR "return to performance" OR "return to level" OR "match fitness" OR "training fitness" OR "full fitness" OR "repetitive injury" OR "recurrent injury" OR "reinjury risk" OR "reinjury" OR "reinjury rate" OR "re-injury" OR "re-injury rate" OR validity OR reliability OR specificity OR sensitivity OR "repetitive sprain" OR "recurrent sprain")
Science Direct	("ankle injuries" or "ankle sprain" or "ankle inversion trauma") **AND** (test OR measurement OR criteria) **AND** ("return to" OR reinjury OR re-injury OR validity OR reliability OR sensitivity OR specificity OR "recurrent sprain" OR fitness OR sport)
SPORTDiscus	("Ankle Injuries" OR "ankle injury" OR "ankle sprain" OR "lateral ankle sprain" OR "ankle inversion trauma") **AND** (test OR "functional test" OR "functional tests" OR "functional testing" OR "static test" OR "mechanical test" OR "clinical test" OR "measurement" OR "criteria") **AND** ("Return to sport" OR "Reproducibility of results" OR "Limit of detection" OR "return to sports" OR "return to play" OR "return to participation" OR "return to action" OR "return to sporting activities" OR "return to activity" OR "return to competition" OR "return to training" OR "sports participation" OR "return to performance" OR "return to level" OR "match fitness" OR "training fitness" OR "full fitness" OR "repetitive injury" OR "recurrent injury" OR "reinjury risk" OR "reinjury" OR "reinjury rate" OR "re-injury" OR "re-injury rate" OR validity OR reliability OR specificity OR sensitivity OR "repetitive sprain" OR "recurrent sprain")

Electronic Supplementary Material Table S2. Clinical assessment tests

Category	**Test/Test battery/Guideline/Index**	**References**
Swelling	Figure-of-eight method	[1,2]
Ligamentous laxity	Anterior drawer test	[2-6]
	Talar tilt test	[2,4]
	Inversion tilt	[4]
	Medial subtalar glide test	[7]
	Talar glide test	[2]
	Posterior-talar glide test	[2]
	Distal fibular position	[5]
Range of motion	Inclinometer	[7]
	Goniometer	[7]

Electronic Supplementary Material Table S3. Functional tests

Category	Test/Test battery/Guideline/Index	References
Proprioception	Biodex systems (joint reposition sense, sense of resistance, sense of kinaesthesia)	8
Hopping and jumping	One-legged hop	8-11
	Square hop test	12
	6 meter crossover hop	12
	Stairs hop	11,13
	Triple hop for distance	11,13
	Figure-8 hop	10,12
	Side-to-side hop	10,12
	Triple-crossover hop for distance	8,10
	Single limb hopping course	8
	6 meter hop for distance	8
	6 meter hop for time	8
	Single-legged jump-landing	14
	Vertical jump test	15
	Vertical drop jump	16
Range of motion	Knee-to-wall test (goniometer); weight bearing lunge test	2,6

Electronic Supplementary Material Table S3. Functional tests – continued

Category	Test/Test battery/Guideline/Index	References
Postural balance	Single-legged postural equilibrium test / Foot lift test / Time in balance test	6,8,9
	Balance test on a computerized board	9,17
	Spring test on an electronic contact platform	9
	One-legged balance test on a square beam	9
	Star excursion balance test	6,18
	Balance error scoring system	19
Agility / speed	Zig zag run	16
	Shuttle run with side steps	16
	Agility t-test	15
	40-meter walk	11,13
	40-meter run	11,13
	Timed up-and-down stair test	6,9
	Modified figure-of-8 running test	9
	Running in a figure-of-8 test	9,11,13
	Walking down a staircase	9
Strength	Isometric dynamometer (invertor – evertor)	20
	Isokinetic dynamometer (invertor – evertor)	6,8
	One-legged rising on heels	9
	One-legged rising on toes	9

Chapter 3: Test-retest, intra- and inter-rater reliability of the reactive balance test in healthy recreational athletes.

Bruno Tassignon

Jo Verschueren

Jonas De Wachter

Alexandre Maricot

Kevin De Pauw

Evert Verhagen

Romain Meeusen

Phys Ther Sport (2020), 46, pp. 47-53.

Abstract

Objective

The reactive balance test (RBT) is a recently developed neurocognitive balance test. The aim of this study was to determine test-retest, intra- and inter-rater reliability of the RBT in healthy recreational athletes.

Design

Reliability study design.

Setting

Primary.

Participants

Twenty-one volunteers (age = 22 ± 1 years, height = 175 ± 9 cm, weight = 69 ± 7 kg) participated.

Interventions

The two experimental trials were separated by an average of 33 ± 15 days. During experimental trials participants performed the Y-balance test (to determine maximal reach distances), and RBT once.

Main outcome measures

Visuomotor response time and accuracy. Test-retest, intra- and inter-rater reliability were estimated for both these RBT outcome measures.

Results

Excellent intra- and inter-rater reliability was observed for visuomotor response time and accuracy. Test-retest reliability for visuomotor response time was considered good, while moderate test-retest reliability was found for accuracy.

Conclusions

Our results indicate that overall test-retest, intra- and inter-rater reliability of the RBT was moderate to excellent. Thus, the RBT possesses acceptable reliability to use in group level analyses. Future research should further determine the clinimetric properties of the RBT in specific populations and research the RBT along the sport injury continuum.

Highlights

1) The reactive balance tests measures visuomotor response time and accuracy.
2) The RBT shows excellent intra- and interrater reliability for both outcomes.
3) Good test-retest reliability was found for RBT visuomotor response time.
4) Moderate test-retest reliability was observed for RBT accuracy.
5) Further research should determine its applicability in clinical practice.

Introduction

Functional performance tests (e.g. hop tests, balance tests) are commonly used by clinicians to screen for sport injury risk, to assess residual impairments after injury, to monitor rehabilitation progress, and to support the return to sport decision-making process. Despite the great number of available tests, the functional performance repertoire can be considered quite distant from the actual sport context as these test solely involve pre-planned motor tasks [1-4]. Even though one of the suggested key drivers for safe and effective sport performance is a person's ability to adapt to a variety of changing conditions [5], a clear absence of functional performance tests integrating adaptability exists. One of the possibilities to measure adaptability in a clinician-friendly way is by adding neurocognitive components (e.g. visuomotor response time, decision-making) to existing functional performance tests. An additional rationale substantiating the development of such neurocognitive functional performance tests can be derived from the association between lower neurocognitive performance and increased lower extremity sport injury risk [6-8].

Within the current functional performance testing repertoire, the Star Excursion Balance Test (SEBT) and Y-balance (YBT) test are the most prevalent due to the tests' ability to reliably assess injury risk and its associated claim to predict injuries [3,9,10]. The SEBT provides information on dynamic balance by measuring maximum reach distances in eight directions whilst the participant has to maintain balance on the contralateral leg [9]. However, more than halve of these reach directions were found to be redundant and led to the development of the YBT which only comprises the three most essential reach directions (i.e. anterior, posteromedial and posterolateral) [10]. Despite good reliability and criterion validity [3], these balance tests neglect the context of balance in relation to open skilled sports performance (e.g. tennis, football) and do not integrate any type of adaptability measures. Recently, the reactive balance test (RBT) was developed and brought the YBT closer to the sports context by adding a neurocognitive task which involves environmental perception, decision-making and the selection of appropriate visuomotor responses while maintaining unilateral balance [11]. Typical neurocognitive outcomes of the RBT encompass visuomotor response time and accuracy. Given that neurocognitive and balance outcome measures are considered important components of sports injury risk and performance [12,13], the RBT might become a valuable addition to the functional performance test repertoire. Nevertheless, the reliability of the RBT has never been researched before. This provides limitations for both researchers and clinicians in correctly interpreting the results of the RBT. An important first step in the potential implementation of the RBT in clinical practice and research is the careful estimation of reliability of the RBT. Therefore, the aim of this study was to determine the test-retest, intra- and inter-rater reliability of the RBT outcomes in recreational athletes.

Materials and methods

We followed the GRRAS guidelines by Kottner, Audige, Brorson, Donner, Gajewski, Hrobjartsson, Roberts, Shoukri, Streiner [14] for reporting reliability. In this manuscript intra-rater reliability should be interpreted as a measure of how consistent an individual is at determining visuomotor response time and accuracy of the RBT, while inter-rater reliability refers to how consistent different individuals are at determining visuomotor response time and accuracy of the RBT. Test-retest reliability denotes how consistent the same outcome measures were determined over time among participants who are assumed not to have changed on the outcome measures being assessed. The objective of this study is to provide information on the internal consistency, intra class coefficients [95% confidence intervals], standard error of measurement, standard error of prediction, minimal detectable change of both RBT visuomotor response time and accuracy for each of the aforementioned reliability measures.

Participants

Since this was the first study to assess the reliability of the RBT, sample size calculation was based upon the mathematical work of Walter, Eliasziw, Donner [15]. A reliability study consisting of two experimental trials (n = 2), a null hypothesis of 0.7, and an alternative hypothesis of 0.9 based on an alpha of 0.05 and a beta of 0.20 would require the inclusion of at least 18 participants (k). Twenty-one healthy recreationally trained athletes (age = 22 ± 1 years, height = 175 ± 9 cm, weight = 69 ± 7 kg) participated in this study. The included recreational athletes had a weekly physical activity level ranging between moderate and high with a total metabolic equivalent of task (MET) of 2746.2 ± 419.4 MET-min/week. They were on average 6.6 ± 3h/day sedentary and participated in at least 1 sport or physical workout at least 2 times per week. The range of practiced sports or physical workouts contained gym based sessions (strength or cardio workouts), running, hockey, rugby, horseback riding, cycling, gymnastics, swimming, squash, CrossFit, rope skipping, tennis, parkour or karate. Participants were excluded if they (1) reported a back or lower extremity injury less than six months prior to the experiment, (2) had any other relevant medical history or current conditions (e.g. neurological diseases, inner ear disorders, color blindness) that could interfere with the balance system or action-perception system, (3) or medication or drug use that could possibly have an effect on balance and visuomotor response time performance. All subjects were asked to refrain from alcohol and caffeine the day before and on the day of each trial, and to not participate in vigorous physical activity 24h prior to each trial. All participants confirmed to have complied with these instructions. Furthermore, all participants were fully informed on the nature and procedures of the study, had the opportunity to ask questions and signed a written informed consent before the trial of the experiment. The experimental protocol was approved by the institutional medical ethics committee of the Vrije Universiteit Brussel and Universitair Ziekenhuis Brussel, Belgium (B.U.N. 143201734045)

Procedures

Test protocol

Participants visited the laboratory three times, once for a familiarization (± 1 h) and twice for an experimental trial (± 30 min). During the familiarization trial both the YBT and RBT were performed six times by the participants, while during both experimental trials the YBT was performed four times and the RBT one time. Figure 1 depicts an overview of the protocol and timeline of subjects' participation. The familiarization trial and first experimental trial were separated by at least one week. Average time between the two experimental trials was 33 ± 15 days ranging from 15 to 68 days. The duration and range of the test-retest time frame was selected in accordance to the study of Greenberg, Barle, Glassmann, Jung [16] in order to attempt to mimic a typical interval between reassessments in a clinical setting to reflect a more "clinically relevant" period. Testing procedures were similar during the familiarization and experimental trials. The YBT protocol as well as the instructions for correct YBT performance were adopted from Plisky, Gorman, Butler, Kiesel, Underwood, Elkins [10] with the added instruction for participants to keep their hands on the hips whilst performing the YBT [9]. The RBT protocol and its instructions were in accordance with the work of Verschueren, Tassignon, Pluym, Van Cutsem, Verhagen, Meeusen [11]. The familiarization trial consisted of participants carrying out the YBT six times on their right leg (stance leg), in order to get to know the procedures and to attenuate learning effects during the experimental trials. Performing 6 repetitions has shown to mitigate possible learning effects in the star excursion balance test and YBT [10,17-19], while a minimum of at least 4 repetitions is necessary to achieve stability in the maximum excursion distances and stance leg angular displacement values [9,20,21]. After being familiarized to the YBT, participants also performed the RBT six times on the same leg. Participants rested for at least 3 minutes between each RBT repetition during the familiarization trial. During the first and second experimental trial, participants carried out the YBT four times on the Y-Balance Test Kit™ to determine maximal reach distance in the anterior, posteromedial and posterolateral directions. Then, eighty percent of a participant's maximal reach distance for each direction was calculated to position the LED lights on the Y-Balance Test Kit™ used during the RBT. The RBT was only carried out one time during each experimental trial. Participants could not be blinded due to the nature of the study.

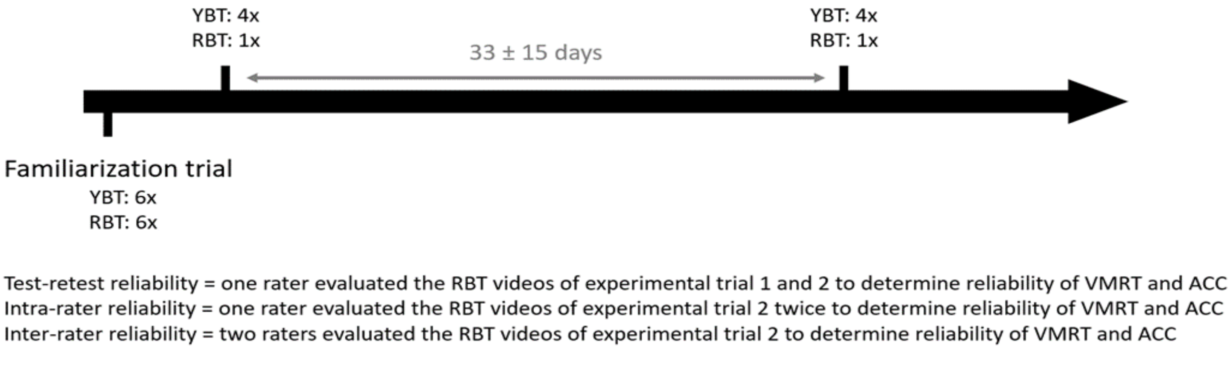

Fig. 1 – Protocol overview and timeline of subject's participation.

Y-balance test (YBT)

The YBT (Y-Balance Test Kit™, FunctionalMovement.com, Danville, VA) encompasses a central stance platform to which three plastic bars are attached in the anterior, posteromedial and posterolateral direction. Each posterior bar is positioned in an angle of 135 degrees from the anterior bar. The angle between the two posterior bars equals 90 degrees. Each bar is marked per 5 millimeters. The participant stood on one leg on the center foot platform with the most distal aspect of the foot and had to push the reach indicators with the free limb along each bar. Afterwards, the reach indicator was left in place, so the researchers could precisely note the reach distance for each direction [10]. A reach was considered successful if the participant abided by the instructions of Plisky and colleagues (2009). A reach was considered unsuccessful if the participant failed to maintain unilateral stance on the platform, failed to maintain reach foot contact with the reach indicator, used the reach indicator for stance support, failed to return to the starting position, or failed to keep the hands on the iliac crest.

Reactive balance test (RBT; see Fig. 2)

The RBT incorporates the Y Balance Test Kit™ in combination with Fitlight™-hardware and software (FITLIGHT Sports Corp, Aurora, Canada). The visuomotor task involves four LED lights: one LED light is placed in front of the YBT while three others are placed on the Y Balance Test Kit™ at 80% of each participant's maximal reach distance. This 80% value was in accordance with the development paper by Verschueren et al. (2019) in order for participants to be able to react in an appropriate way, while also sufficiently stressing participants' balance control. The LED light in front of the Y Balance Test Kit™ emits for 0.2 seconds (s) one of three predetermined colors (red, blue, or green), and is always followed instantaneously by a 2 s color-matched LED light attached to the Y Balance Test Kit™. Participants were instructed to react to this visual stimulus as fast as possible by extinguishing the correct LED light attached to the YBT without losing balance. Participants had to pass over the LED light within a range of 5 cm with one's foot in order to achieve this. Each axis corresponds to a predetermined and fixed color: the color blue indicated that the participant needed to reach forward along the anterior axis, while the green color was placed along the posteromedial axis and the red color along the posterolateral axis. For example, if the LED light in front of the YBT turned green, the participant had to extinguish the posteromedial LED light. Visuomotor response time was registered and automatically saved on a tablet by the Fitlight™-software. Randomization of color sequence and interstimulus times were programmed according to the RBT test protocol [11]. The colors red, blue or green were each presented 12 times, resulting in a total of 36 stimuli. The total duration of one trial of the RBT is about 1min30s to 2 min. To avoid possible learning effects the inter-stimulus time varied between 1.5, 2, or 2.5 s, and each inter-stimulus time was randomly used 12 times. Furthermore, the starting point of the color sequence was also randomized for every performed trial, so participants could not memorize the color sequence, nor the inter-stimulus times. Outcome measures of the RBT were visuomotor response time (ms) and accuracy (%). In accordance with the article of Verschueren and colleagues (2019), each RBT trial was filmed with a video camera (Handycam 1080 50i, HDR-CX105E, Sony Corporation, Japan) in order to retrospectively determine accuracy and correct visuomotor response time through video analyses. When analyzing the RBT videos, raters noted missed stimuli, multiple attempts needed, decision errors and balance errors for each participant. All errors were taken into account for both visuomotor response time and accuracy. The accuracy score was determined as follows: Accuracy (%) = ((Total number of stimuli – (missed stimuli + multiple attempts needed + decision errors)) / Total number of stimuli) x 100. Definitions of all these errors can be found in Table 1.

Table 1 – Definitions of accuracy errors

Error	Definition
Missed stimulus	The participant failed to extinguish the LED light
Multiple attempts	The participant is reaching from the standardized position, but failed to extinguish the LED light the first time. The participant needed two or more attempts
Decision error	The participant initiated movement in the wrong direction
Balance error	- The participant did not start from the standardized position at stimulus onset - The participant is trying to find balance during reach - The participant needs to put a hand or foot on the floor - The participant steps off the YBT Test kit - The participant is not able to keep the hands on the hips - The participant lifts the forefoot or heel off the testing surface

Visuomotor response time was subsequently corrected for accuracy errors by removing the corresponding visuomotor response time values from the original Fitlight™ Excel data sheet and recalculating the mean visuomotor response time with only the correct extinguished LED lights included.

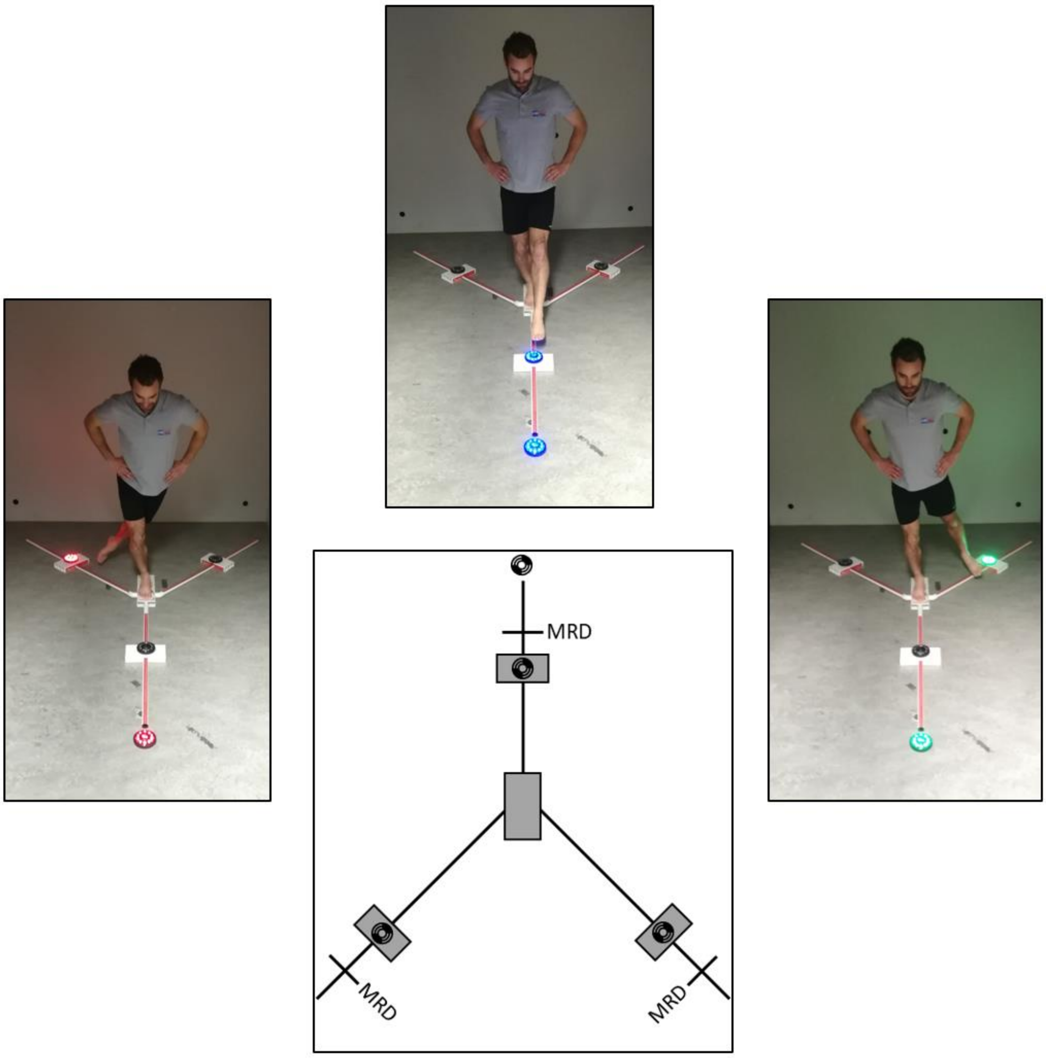

Fig. 2 – Reprinted with permission from Verschueren et al. (2019). Reactive balance test. MRD = Maximal Reach Distance; ◎ = Fit-light trainer LED-lights.

<u>Raters</u>

The two raters (AM, JDW) had experience with the RBT and were trained in the evaluation of the RBT accuracy and visuomotor response time analysis. Intra-rater reliability was estimated by one rater (AM) by evaluating the RBT videos of the second experimental trial twice. The rater was blinded for his second evaluation and performed this evaluation at least two weeks after the first evaluation. Inter-rater reliability was calculated by comparing both raters' evaluations of the RBT videos of the second experimental trial. Raters were blinded for each other's evaluation. Data of the RBT videos of experimental trials one and two were compared to determine test-retest reliability and was performed by one rater (AM).

Statistical Analysis

All statistical tests were conducted using the Statistical Package for the Social Sciences, version 26 (SPSS Inc., Chicago, IL, USA). Internal consistency (Cronbach α), intraclass correlation coefficient (ICC), standard error of measurement (SEM), standard error of prediction (SEP) and minimal detectable difference (MDD) were outcomes of interest when calculating random error scores for both visuomotor response time and accuracy test-retest, intra- and inter-rater reliability. The guidelines of Koo & Li (2016) were consulted in order to select the appropriate model, type, and definition of relationship for the used ICC. ICC (3, 1) was used to estimate intra-rater and test-retest reliability, while ICC (2, 1) was selected for calculating inter-rater reliability. ICC values less than 0.5 were considered indicative of poor reliability, values between 0.5 and 0.75 indicated moderate reliability, values between 0.75 and 0.9 indicated good reliability, and values greater than 0.90 indicated excellent reliability [23]. SEM ($= SD \times \sqrt{(1 - ICC)}$) was calculated to estimate the variability of the measured scores likely to be obtained given a participant's true score [24]. SEP ($= SD \times \sqrt{(1 - ICC^2)}$) was calculated to gain insight on the estimate of variability of a participant's actual score when performing a test a second time, given their performance on the first test [24]. MDD ($= Z_{95\%} \times SEP \times \sqrt{2}$) was calculated to determine what would constitute of a real change in RBT performance [24-27].

Results

Table 2 provides an overview of Cronbach α, ICC [95% CI], SEM, SEP, and MDD for test-retest, intra- and inter-rater reliability. The mean (± standard deviation) total duration of one RBT trial was 1min45s ± 4s. For intra-rater reliability, rater one estimated a mean ± standard deviation visuomotor response time of 766.09 ± 113.43 ms for the first evaluation and 765.63 ± 114.82 ms for the second evaluation, while an accuracy of 90.72 ± 6.76 % was observed for the first evaluation and 89.92 ± 7.27 % for the second evaluation. In terms of test-retest reliability, participant obtained a visuomotor response time of 759.59 ± 126.49 ms during the first trial and 766.09 ± 113.43 ms during the second trial. The mean accuracy during the first trial was 90.98 ± 6.74 % and 90.72 ± 6.76 % during second trial. Regarding inter-rater reliability, rater one estimated a visuomotor response time of 766.09 ± 113.43 ms and an accuracy of 90.72 ± 6.76 %, while rater two found a visuomotor response time of 722.21 ± 68.43 ms and an accuracy of 90.34 ± 7.06 %.

Excellent intra- rater reliability was observed for visuomotor response time (ICC: 0.992, [0.981; 0.997]) and accuracy (ICC: 0.925, [0.827; 0.969]). Excellent inter-rater reliability was also observed for both visuomotor response time (ICC: 0.978, [0.946; 0.991]) and accuracy (ICC: 0.920, [0.803; 0.968]). Test-retest reliability for visuomotor response time could be considered good (ICC: 0.831, [0.629; 0.928]), while moderate test-retest reliability was found for accuracy (ICC: 0.706, [0.420; 0.820]).

Table 2: data overview and corresponding reliability

	Cronbach α	ICC	ICC 95% CI	SEM	SEP	MDD
Intra-rater reliability						
VMRT	0.996	0.992	(0.981; 0.997)	10.15	14.32	39.69
ACC	0.963	0.925	(0.827; 0.969)	1.85	2.57	7.12
Test-retest reliability						
VMRT	0.904	0.831	(0.629; 0.928)	51.59	69.81	193.51
ACC	0.747	0.706	(0.420; 0.820)	4.23	5.36	14.86
Inter-rater reliability						
VMRT	0.980	0.978	(0.946; 0.991)	16.83	23.66	65.59
ACC	0.917	0.920	(0.803; 0.968)	1.91	2.65	7.35

VMRT = visuomotor response time (in ms); ACC = accuracy (in %); SD = standard deviation; ICC = intraclass correlation coefficient;

ICC CI = 95% confidence interval of the intraclass correlation coefficient; SEM = Standard Error of Measurement;

SEP = Standard Error of Prediction; MDD = Minimal detectable difference

Discussion

The current study is the first to determine the test-retest, intra- and inter-rater reliability of the RBT outcomes. Excellent intra-rater reliability for both visuomotor response time and accuracy demonstrated that a rater was very consistent in evaluating the RBT videos with at least two weeks in between evaluations whilst also being blinded for his first evaluation of the same videos. Given this consistency, one can confidently interpret the test-retest reliability of the RBT. Over time RBT visuomotor response time shows good reliability, while RBT accuracy possesses moderate reliability meaning that the RBT is fairly consistent over time. When multiple raters independently assessed the RBT, excellent reliability for both visuomotor response time and accuracy indicate that different raters can consistently evaluate the same RBT trial.

In accordance with the recommendations of the *scientific advisory committee of the medical outcomes trust*, minimal standards for test-retest ICCs in order to be able to use a measuring instrument for group level analyses over time are typically considered to be ≥ 0.70, while ICCS between 0.90 and 0.95 are considered for individual level analyses and decision-making over time [23,28]. When extrapolating these recommendations to the current study, the test-retest reliability results imply that the RBT possesses acceptable reliability for visuomotor response time and accuracy to use in group level analyses or follow-up measures, for instance in scientific research. Even though intra- and inter-rater reliability were both excellent for visuomotor response time and accuracy, higher intra-rater reliability scores were obtained compared to inter-rater reliability scores resulting in marginally lower SEM, SEP and MDD scores. Therefore, it is recommended to always let the same rater evaluate the RBT. However, if this would not be practically possible, other raters can always be involved to determine RBT visuomotor response time and accuracy. Regarding the current applicability of the RBT in individual analyses, the RBT might not be optimally suited for such purpose within a generic recreationally trained population. Therefore, future research should determine the reliability in more specific populations in order to provide a better insight whether or not the RBT would be suited for these specific populations for individual screening, monitoring, follow-up and decision-making in clinical practice.

Current clinician-friendly functional performance tests used in the injury prevention, rehabilitation or return to sport decision-making domain focus on assessing aspects of physical performance and movement quality in a closed environment without any additional neurocognitive load. Nevertheless, the importance of bringing functional performance tests closer to the sports context and adding neurocognitive load in a standardized way has been evidenced by the recent development of different neurocognitive functional performance tests. Besides the development of the RBT by Verschueren and colleagues (2019), Millikan, Grooms, Hoffman, Simon [29] developed and researched the reliability of four neurocognitive hop tests. They added various visuomotor tasks to already existing hop tests and found good to excellent test-retest reliability. This is in line with our results, and indicates that neurocognitive functional performance tests can be implemented in research. The main rationale for adding neurocognitive components to the current functional performance test repertoire is that lower neurocognitive performance as well as adding cognitive load to physical performance have been associated with an increased sport injury risk [6-8,30,31]. The development of these new functional performance tests is hopeful for both clinicians and researchers, as they could offer innovative ways to assess patients' and participants' functional performance within the injury prevention, rehabilitation and return to sport decision-making domain. Nevertheless, clinicians and researchers would have to purchase a visuomotor-hardware and -software system and potential additional equipment (e.g. YBT Test Kit) in order to be able to perform neurocognitive performance tests. Such equipment, and especially the used visuomotor-hardware and -software system in this study requires a relatively high financial investment. Even though clinicians could consider using these neurocognitive functional performance tests and their visuomotor systems as an extension of their current exercises for patients in the meantime, the cost-effectiveness as well as the practical applicability should be carefully considered before purchasing such or cheaper visuomotor systems. Furthermore, extensive research is warranted before neurocognitive functional performance tests could potentially be considered for and integrated in day-to-day clinical practice.

Limitations and future research

A limitation of this study was the athletic ability and fitness level of the participants as they were recreationally trained individuals. This may have consequences for the interpretation of the results, since ICC estimation is dependent on and specific to the used population. Future research should therefore assess the reliability and other clinimetric properties (e.g. construct validity, minimal clinically important difference) in other populations, such as elite athletes and patient populations (e.g. ankle sprain injury, anterior cruciate ligament injury). Also, populations and contexts outside sports should be considered, for instance patients with cognitive impairments or balance disorders, patients with movement impairments or neurological diseases/impairments (children to adults), within the pediatric or geriatric context, military, performance arts, physical fitness test batteries, etc.. Furthermore, the duration of the total RBT procedure (i.e. YBT, determining LED-light distance, RBT, analysis of results) could be considered quite lengthy and difficult to implement for clinicians in their daily practice life. Therefore, test developers, researchers and clinicians should explore potential cheaper and less time-consuming (e.g. reduce total number of stimuli) options for already existing and new neurocognitive performance tests in order to be able to offer more time-efficient, cost-effective and clinician-friendly tests. Additionally, not all aspects of adaptability and neurocognition can be captured by the RBT, since the RBT is not able to recreate an open sports environment. Nevertheless, the addition of a standardized continuous neurocognitive task to the YBT as well as the selected associated injury risk outcome measures of the RBT could add value to clinical studies encompassing functional performance tests. Therefore, prospective clinical studies should determine whether the RBT and other neurocognitive functional performance tests would be useful when screening for sport injury risk, assessing residual impairments post-injury, monitoring rehabilitation progress, and supporting the return to sport decision-making process.

Conclusion

In recreationally trained individuals, the RBT possesses excellent intra- and inter-rater reliability. In terms of test-retest reliability RBT visuomotor response time could be considered good, while moderate test-retest reliability was found for accuracy. These results imply that the RBT possesses acceptable reliability to use in group level analyses or follow-up measures in research.

References

1. Hegedus EJ, McDonough S, Bleakley C, Baxter GD, DePew JT, Bradbury I, et al. Physical performance tests predict injury in National Collegiate Athletic Association athletes: a three-season prospective cohort study. Br J Sports Med. 2016 Nov;50(21):1333-7.

2. Tassignon B, Verschueren J, Delahunt E, Smith M, Vicenzino B, Verhagen E, et al. Criteria-based return to sport decision-making following lateral ankle sprain injury: a systematic review and narrative synthesis. Sports Med. 2019 Feb 11;49(4):601-19.

3. Hegedus EJ, McDonough SM, Bleakley C, Baxter D, Cook CE. Clinician-friendly lower extremity physical performance tests in athletes: a systematic review of measurement properties and correlation with injury. Part 2-the tests for the hip, thigh, foot and ankle including the star excursion balance test. Br J Sports Med. 2015 May;49(10):649-56.

4. Chimera NJ, Warren M. Use of clinical movement screening tests to predict injury in sport. World Journal of Orthopedics. 2016 Apr;7(4):202-17.

5. Glasgow P, Bleakley CM, Phillips N. Being able to adapt to variable stimuli: the key driver in injury and illness prevention? Br J Sports Med. 2013 Jan;47(2):64-5.

6. Wilkerson GB, Mokha M. Neurocognitive reaction time predicts lower extremity sprains and strains. IJATT. 2012 Nov;17(6):4-9.

7. Swanik CB, Covassin T, Stearne DJ, Schatz P. The relationship between neurocognitive function and noncontact anterior cruciate ligament injuries. American Journal of Sports Medicine. 2007 Jun;35(6):943-8.

8. Herman DC, Barth JT. Drop-Jump Landing Varies With Baseline Neurocognition: Implications for Anterior Cruciate Ligament Injury Risk and Prevention. American Journal of Sports Medicine. 2016 Sep;44(9):2347-53.

9. Gribble PA, Hertel J, Plisky P. Using the star excursion balance test to assess dynamic postural-control deficits and outcomes in lower extremity injury: a literature and systematic review. J Athl Train. 2012 May-Jun;47(3):339-57.

10. Plisky PJ, Gorman PP, Butler RJ, Kiesel KB, Underwood FB, Elkins B. The reliability of an instrumented device for measuring components of the star excursion balance test. N Am J Sports Phys Ther. 2009 May;4(2):92-9.

11. Verschueren J, Tassignon B, Pluym B, Van Cutsem J, Verhagen E, Meeusen R. Bringing context to balance: development of a reactive balance test within the injury prevention and return to sport domain. Arch Physiother. 2019.

12. Brachman A, Kamieniarz A, Michalska J, Pawlowski M, Slomka KJ, Juras G. Balance training programs in athletes - a systematic review. J Hum Kinet. 2017 Sep;58(1):45-64.

13. Nuri L, Shadmehr A, Ghotbi N, Moghadam BA. Reaction time and anticipatory skill of athletes in open and closed skill-dominated sport. Eur J Sport Sci. 2013 Sep;13(5):431-6.

14. Kottner J, Audige L, Brorson S, Donner A, Gajewski BJ, Hrobjartsson A, et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. J Clin Epidemiol. 2011 Jan;64(1):96-106.

15. Walter SD, Eliasziw M, Donner A. Sample size and optimal designs for reliability studies. Stat Med. 1998 Jan 15;17(1):101-10.

16. Greenberg ET, Barle M, Glassmann E, Jung MK. Interrater and test-retest reliability of the y balance test in healthy, early adolescent female athletes. Int J Sports Phys Ther. 2019 Apr;14(2):204-13.

17. Hertel J, Miller SJ, Denegar CR. Intratester and intertester reliability during the star excursion balance tests. J Sport Rehabil. 2000 May;9(2):104-16.

18. Linek P, Sikora D, Wolny T, Saulicz E. Reliability and number of trials of Y Balance Test in adolescent athletes. Musculoskelet Sci Pract. 2017 Oct;31:72-5.

19. Shaffer SW, Teyhen DS, Lorenson CL, Warren RL, Koreerat CM, Straseske CA, et al. Y-Balance Test: A Reliability Study Involving Multiple Raters. Military Medicine. 2013 Nov;178(11):1264-70.

20. Robinson RH, Gribble PA. Support for a reduction in the number of trials needed for the star excursion balance test. Archives of physical medicine and rehabilitation. 2008 Feb;89(2):364-70.

21. Coughlan GF, Fullam K, Delahunt E, Gissane C, Caulfield BM. A comparison between performance on selected directions of the star excursion balance test and the Y balance test. Journal of athletic training. 2012 Jul-Aug;47(4):366-71.

22. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016 Jun;15(2):155-63.

23. Portney L, Mary W. Foundations of clinical research: applications to practice. 3 ed. Upper Saddle River, New Jersey 07458: Pearson Education, Inc.; 2009.

24. McManus IC. The misinterpretation of the standard error of measurement in medical education: a primer on the problems, pitfalls and peculiarities of the three different standard errors of measurement. Med Teach. 2012;34(7):569-76.

25. Dudek FJ. The continuing misinterpretation of the standard error of measurement. Psychol Bull. 1979;86(2):335-7.

26. Charter RA. Revisiting the standard errors of measurement, estimate, and prediction and their application to test scores. Percept Mot Skills. 1996 Jun;82(3):1139-44.

27. Weir JP. Quantifying test-retest reliability using the intraclass correlation coefficient and the SEM. J Strength Cond Res. 2005 Feb;19(1):231-40.

28. Aaronson N, Alonso J, Burnam A, Lohr KN, Patrick DL, Perrin E, et al. Assessing health status and quality-of-life instruments: attributes and review criteria. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2002 May;11(3):193-205.

29. Millikan N, Grooms DR, Hoffman B, Simon JE. The development and reliability of four clinical neurocognitive single-leg hop tests: implications for return to activity decision making. J Sport Rehabil. 2018 Nov 14:1-26.

30. Brown TN, Palmieri-Smith RM, McLean SG. Sex and limb differences in hip and knee kinematics and kinetics during anticipated and unanticipated jump landings: implications for anterior cruciate ligament injury. Br J Sports Med. 2009 Dec;43(13):1049-56.

31. Seymore KD, Cameron SE, Kaplan JT, Ramsay JW, Brown TN. Dual-task and anticipation impact lower limb biomechanics during a single-leg cut with body borne load. J Biomech. 2017 Dec 8;65:131-7.

Chapter 4: Mental fatigue impairs clinician-friendly balance test performance and brain activity.

Bruno Tassignon

Jo Verschueren

Kevin De Pauw

Bart Roelands

Jeroen Van Cutsem

Evert Verhagen

Romain Meeusen

Transl Sports Med (2020), 3, pp. 616-625.

Abstract

Purpose

While mental fatigue (MF) increases the probability of losing balance, the underlying neural mechanisms remain to be studied. Balance is commonly represented by technical outcomes difficult to translate to clinical practice. Therefore, the aims of this study were to assess how MF affects clinician-friendly balance tests and if MF interacts with brain activity during these tests.

Methods

Twelve healthy recreational athletes (age = 23 ± 2 years) participated. MF was induced by a 90-min Stroop test, while the control task encompassed a time-matched documentary. Two clinician-friendly balance tests (i.e. Y-balance test (YBT), reactive balance test (RBT) were performed before and after the 90-min tasks. Brain activity was measured using electroencephalography during YBT and RBT.

Results

MF significantly decreased RBT accuracy compared to pre-MF and compared to post-control. MF did not affect YBT performance and visuomotor reaction time on the RBT. During the YBT, MF significantly induced higher prefrontal cortex theta activity. Brain activity during the RBT remained unchanged post-MF.

Conclusion

MF impairs RBT performance, but no underlying brain activity changes were observed. In contrast, YBT performance did not change due to MF, but alterations in brain activity during YBT performance were in line with previous MF research.

Introduction

Mental fatigue can be defined as a psychobiological state that emerges during or after periods of prolonged cognitive activity [1]. This state can manifest subjectively, physiologically and behaviourally. At the subjective level, mental fatigue is logically characterized by an increase in self-reported feelings of mental fatigue (e.g. measured by a visual analogue scale (M-VAS) [2-4]. At the physiological level, several recurring brain activity changes have already been recorded by means of electroencephalography (EEG) as a consequence of mental fatigue (i.e. increased theta and alpha brain activity) [2,4-9]. Behaviourally, mental fatigue has recently been associated with multiple impairments in physical performance [1]. Impairments when mentally fatigued have primarily been found in endurance performance, psychomotor skills, balance, neurocognitive performance (slower visuomotor response time and lower accuracy) and decision-making [1,2,4-8,10,11]. However, the underlying neurophysiological mechanisms of these performance impairments still remain to be elucidated. In terms of mental fatigue and human balance control, Lew et al. (2014) and Qu et al. (2019) found that mental fatigue interfered with human balance control and increased the probability of losing balance [10,11]. These findings further substantiate the increasing body of scientific evidence that indicates that the brain's neocortex is essential in human balance control [12,13]. Furthermore, it also triggers the question which specific role the brain plays in this impairment in balance control when mentally fatigued. Nonetheless, to the best of the authors' knowledge, no studies examined the effects of mental fatigue on brain activity during balance tasks.

Besides the need to further fundamentally explore how mental fatigue affects balance and its underlying neural correlates, a great challenge exists to bring fundamental research closer to clinical practice. Up till now, the construct of balance has commonly been represented in fundamental research by biomechanical and technical outcome measures that are difficult to apply in clinical practice and directly support clinicians [10-13]. Therefore, commonly used and clinician-friendly balance tasks should be encapsulated in research with the aim of bridging the gap between the lab and clinical practice. For instance, the Y-balance test (YBT) is commonly used in clinical practice and is often included in the screening for lower extremity sport injury risk [14-16]. Given that also lower neurocognitive performance has been associated with an increased lower extremity sport injury risk [17-19], we recently developed the reactive balance test (RBT). The RBT allows practitioners and researchers to add neurocognitive components (i.e. visuomotor reaction time, accuracy) to the YBT in an easy and standardized way to further approximate the sport context [20]. The relevance to test mental fatigue in a clinical (sport injury) context is further supported by the statement of athletes claiming to often encounter mental fatigue and it limiting their ability to perform optimally [21,22]. It might thus be of interest for clinicians to know whether or not mental fatigue is able to influence YBT or RBT performance and get insight in how mental fatigue interacts with the brain whilst performing these clinician-friendly balance tests.

Therefore, the aim of the current study was twofold. First, to assess how mental fatigue affects clinician-friendly balance test performance (i.e. YBT, RBT). Secondly, to examine the interaction of mental fatigue with underlying brain activity assessed by means of EEG during these clinician-friendly balance tests. We hypothesized mental fatigue to impair performance on both balance tests and to induce undesirable electrophysiological brain activity changes during balance test performance (i.e. increase in theta and alpha activity).

Materials and methods

Participants

We used G*Power 3.1.9.4-software [23] to conduct a sample size calculation based on the study of Van Cutsem et al. (2018) [3]. They reported a partial eta squared effect size of mental fatigue on a neurocognitive visuomotor task ($\eta^2 = 0.197$). The sample size calculation showed that a minimum of 11 participants had to be included in order to observe an effect of mental fatigue on a neurocognitive visuomotor task. In total, twelve healthy recreative athletes (four women; mean ± SD; age = 23 ± 2 years; height = 175.6 ± 8.7 cm; weight = 68.3 ± 9.9 kg; BMI = 22.1 ± 2.1) participated in the current study. All participants gave written informed consent prior to the study. However, the informed consent concealed the true aim of the study and stated that the purpose of the study was to assess the difference between two cognitive tasks on brain activity during balance performance in order to blind the participants for the specific fatigue hypotheses. Once a participant completed the study, we immediately informed them about the real goals and hypotheses. Participants were only included if they did not use medication and were at least six months injury-free before participating in the experiment. Participants had to abide by the following criteria for each trial: (a) refraining from heavy physical efforts 24 hours prior to the trials, (b) no intake of caffeine-containing or alcoholic beverages 24 hours before and during the trials, and (c) consumption of the same meal the evening and morning before each trial. These criteria were assessed with a pre-trial checklist before each trial. When a participant did not meet these criteria, the trial was rescheduled to another day. The Medical Ethics Committee of the UZ Brussel and research council of the Vrije Universiteit Brussel, Belgium (B.U.N. 143201836625) approved the experimental protocol and procedures.

Experimental protocol (see Figure 1)

We utilized a randomized counterbalanced cross-over design. Participants visited the lab three times. Trials were always separated by a minimum of one week to assure full recovery from the previous trial. For each participant, the first trial was the familiarization trial, while the following two trials consisted of a control and an experimental trial in a randomized order. We used a random number generator to determine the order of the experimental and control trials. All trials, except the familiarization trial, took place at the same time of day (8:00 am or 10:30 am). The familiarization trial encompassed gathering participants' characteristics (i.e. age, height, weight, scalp circumference), fitting an appropriate EEG cap to the participant's head, explaining the proper execution of the balance tests and cognitive tasks, as well as providing further explanations on the questionnaires and measuring scales (i.e. pre-checklist, motivation scale, Visual Analogue Scale for Mental Fatigue, National Aeronautics and Space Administration Task Load Index). More information on these questionnaires and measuring scales can be retrieved in the study of Van Cutsem et al. (2020) [24], since we used identical questionnaires and measuring scales. We selected two clinician-friendly balance tests for this study: (1) the Y-balance test (YBT) because of its widespread use as a dynamic balance test in clinical practice and its relation to the occurrence of lower extremity injuries [14-16], and (2) the reactive balance test (RBT) due to its resemblance to the YBT and its ability to integrate neurocognitive components (e.g. decision-making, visuomotor reaction time, accuracy) in a standardized manner while maintaining balance. During the familiarization trial, participants had to perform both the YBT and RBT at least six times while wearing the full EEG equipment in order to attenuate learning effects during the experimental and control trial. Next, participants practiced the cognitive tasks: the Eriksen Flanker task and a progressive 100% incongruent Stroop Colour Word Test in accordance with the familiarisation trial description of Van Cutsem and colleagues (2020) [24]. At the end of the familiarization trial, participants selected a documentary of their choice to avoid boredom and warrant mental engagement during the control trial. Participants could choose between the following documentaries: 'Planet Earth: as you've never seen it before (the complete series)', 'Eyewitnesses' (Volcanoes, Sharks, Dogs, Apes) or 'Best of Discovery Channel' (When we left earth – The Nasa missions).

The experimental and control trials were identical, except for the 90-minutes 100% incongruent Stroop Colour Word Test and the 90-minute documentary (see fig 1). Mental fatigue was induced by means of the Stroop test (= experimental task), while the control task encompassed watching a time-matched documentary. All trials lasted about two hours and thirty minutes. The experimental and control trials proceeded as follows: before each trial started, participants completed the pre-trial checklist. When the participant met all the criteria of the pre-trial checklist, the researchers placed the EEG cap on the participant's head and started preparing the EEG cap for recording. In the meantime, the participant filled in the motivation scale [25] and the Visual Analogue Scale for Mental Fatigue (M-VAS). Next, baseline EEG measurements and EEG measurements during YBT and RBT were taken. Details on EEG properties, recording and analysis can be found in the *EEG recording and analysis* section. The balance test protocols are described below the *clinician-friendly balance test* subheading. Immediately after the RBT, participants had to indicate their perceived mental fatigue using the M-VAS and completed a three-minute Eriksen Flanker task before starting the experimental or control task. More information on the cognitive tasks (i.e. Flanker task, Stroop Colour Word Test) can be retrieved in the study of Van Cutsem et al. (2020), since identical cognitive tasks were used [24]. During the execution of the experimental and control task, a member of the research team always sat behind the participant to make sure the participant was fully engaged in the task throughout the 90 minutes. Instantly after the experimental or control task, another Eriksen Flanker task was carried out, the perceived mental fatigue was scored and within one minute the participant performed another YBT and RBT while EEG was being recorded. Afterwards, the participant filled in the M-VAS one last time, as well as their subjective workload with the National Aeronautics and Space Administration Task Load Index (NASA-TLX).

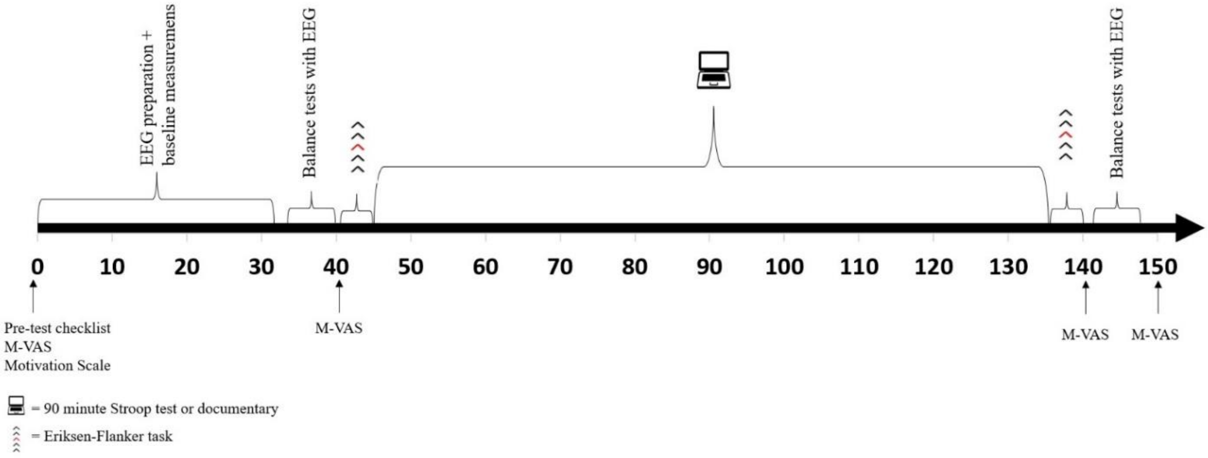

Figure 1 - Overview of the study protocol. M-VAS = perceived mental fatigue scale. EEG = electroencephalography

Clinician-friendly Balance Tests

Y Balance test (YBT)

We used the Y-Balance Test Kit™ from Functional Movement Systems (FMS, Virginia, USA) and instructed participants to maximally push the three reach indicators along its axes (anterior, posteromedial, and posterolateral), while maintaining balance on the dominant leg. All instructions concerning the execution of the YBT were extracted from the study by Plisky et al. (2009) [26], and were complemented with the following instructions in order to minimize EEG movement artefacts: (1) to keep the hands on the pelvis and (2) to keep the head and torso as stationary as practically possible. Outcome measures for each axis of the YBT was the maximal reach distance. In order to obtain reliable maximal reach distances and have a sufficient amount of EEG recording time, participants performed the YBT four times (= 2 minutes equivalent) both at the beginning and at the end of the trial.

Reactive Balance test (RBT)

The goal of this test is to react as fast as possible to extinguish the correct axis-bound LED-light with your foot by passing over the light sensor of the LED-light while maintaining balance on the contralateral leg. The RBT consists of 4 LED-lights (Fitlights™, FITLIGHT Sports Corp., Aurora, Ontario, Canada): three are placed along the three axes of the Y-Balance Test Kit™ and one is placed in front of the YBT and serves as an indicator for the reach direction. Instructions and protocol were in accordance with Verschueren et al. (2019) [20]. A total of 45 stimuli were presented to obtain a test duration of at least 2 minutes. To minimize EEG movement artefacts, participants were asked (1) to keep the hands on the pelvis and (2) to keep the head and torso as stationary as practically possible. The two main outcome measures of the RBT are accuracy (ACC) and visuomotor reaction time (VMRT). VMRT was automatically saved by computer software. For determining ACC, participants were filmed while performing the RBT in order to be able to perform a retrospective visual analysis of missed stimuli, multiple attempts and decision errors. We calculated ACC as: “Total number of stimuli – (missed stimuli + multiple attempts needed + decision errors))/100”. A missed stimulus is defined as ‘participant failed to extinguish LED-light’. Multiple attempts are defined as “reaching from standardized position, but failed to extinguish the LED-light from the first time” and a decision error is defined as “initiating movement in wrong direction/towards a wrong LED-light”. The ACC score was also taken into account for the correction of the VMRT outcomes.

EEG recording and analysis

Brain activity was recorded during baseline measurements and the balance tasks. Baseline measures encompassed sitting 2 min with eyes closed and 2 min with eyes open. These were followed by EEG recordings during YBT (2min) and RBT (2 min at least) performance. Thirty-two active Ag/AgCl electrodes were attached to the fitted EEG cap (actiCAP, Brain Products, Munich, Germany) in accordance with the “10–20 International System” [27], and connected to the amplifier (BrainAMP DC, Brain Products, Munich, Germany). The sampling rate was set at 500 Hz (Brain Vision Recorder, Brain Products, Munich, Germany). Electrode impedance was kept below 10 kΩ throughout the recordings. During EEG recordings, participants inserted earplugs, and were instructed to minimize movement of the head and trunk, to avoid frowning, and to not touch their head in order to attenuate sound, muscle and movement artefacts respectively.

Brain Vision Analyzer software (version 2.2) was used to (pre-)process the data sets. Bad channels were removed by visually inspecting the data and using statistical measures (i.e. kurtosis). Raw data were re-referenced to an average reference and down-sampled to 256 Hz. Infinite Impulse Response Filters were set at 0.1 Hz (high pass), 45 Hz (low pass) and 48 dB/oct (Notch) with a Butterworth Zero Phase Filter design. Raw data inspection was carried out by means of manual artefact removal (i.e. electrode shifts, severe muscle artefacts). Next, Independent Component Analysis (Classic sphering, Extended Biased Infomax) allowed us to extract periodically recurring artefacts (i.e. eye and muscle artefacts) from the data. Since average-referenced data were used for Independent Component Analysis (ICA), these channels were excluded from the analysis to optimally process independent components. The scalp maps, time course of the components and the activity power spectrum were checked to determine whether the independent component was an artefact or brain-related. Scalp topography was accounted for channel noise, meaning that the independent component was removed from the dataset when the weighting was set on a single channel. Furthermore, the time course, matrix of weights and topographies were taken into account in order to remove bad components. The remaining good independent components were projected back to the original EEG signals.

Spectral power analysis

We extracted 4-s segments with an overlap of 2 s for each continuous EEG data set [3]. Fast Fourier transform (FFT) spectral power with a spectral resolution of 0.25 Hz was calculated for each segment. These FFT segments were averaged to stabilize the spectral content. The spectral power was exported for theta (θ, 4–7.75 Hz), alpha (α1, 8–10 Hz; α2, 10.25–12.75 Hz), and beta (β1, 13–18 Hz; β2, 18.25–21 Hz; β3, 21.25–30

Hz) in each region of interest. The prefrontal cortex (PFC), motor cortex (MC) and posterior parietal cortex (PPC) were selected as regions of interest in accordance with the systematic review of Wittenberg and colleagues (2017) [12] and because they play a vital role in dynamic balance and voluntary movement [28]: the prefrontal cortex (FP1, FP2, F3, Fz, F4), motor cortex (FC1, FC2, C3, Cz, C4) and posterior parietal cortex (CP1, CP2, P3, Pz, P4). The PFC is important for attention, decision-making, and predicting the outcome of actions; the MC is mainly involved in motor planning, and the control and execution of voluntary movements; the PPC is mostly engaged in spatial relations, attention, and motor planning [28].

Brain imaging: source localisation

We extracted 4-s segments with no overlap for each continuous EEG data set and averaged these segments. Next, the data was exported to a .dat file for further analysis in the program standardized low resolution brain electromagnetic tomography (LORETA^{KEY}). All procedures were in accordance with the open source LORETA manual concerning the analysis of EEG data. Information of the electrode positions were defined in a transformation matrix (.spinv) file. Each .txt file was converted to one cross spectrum (.crss) file and a standardized low resolution brain electromagnetic tomography (.slor) file for statistical analysis.

Statistical Analysis

The Statistical Package for the Social Sciences, version 26 (SPSS Inc., Chicago, IL, USA) was used to perform the statistical analysis. The critical alpha was set at 0.05 and 95% confidence intervals were used for all analyses. Data are presented as mean values and standard error (SE) unless stated otherwise. We used the Shapiro-Wilk test and visual interpretation of histograms to verify whether data was normally distributed. In case data was not normally distributed square root transformation was used in order to achieve normal distribution (i.e. Eriksen-Flanker accuracy, Stroop accuracy). When data remained not normally distributed after square root transformation (i.e. NASA-TLX frustration subscale), the original data were analysed with non-parametric Wilcoxon signed rank tests. When data were normally distributed, a repeated measure analysis of variance (RM ANOVA) was carried out. Before interpreting RM ANOVA statistical outcomes, sphericity was verified by the Mauchly's test (when applicable). When the assumption of sphericity was violated (lower than 0.75), RM ANOVA outcomes were interpreted following the Greenhouse-Geiser procedure. The significance level, F-ratios and effect sizes (partial eta square) were taken into account when interpreting the statistical outcomes. If RM ANOVA outcomes showed a significant interaction effect, subsequent RM ANOVA analyses or post hoc paired t-tests were used to examine the effect of time and condition. In case of no significant interaction effect, the main effect of time and condition were interpreted. A (2x2) RM ANOVA was selected to analyse the effect of condition (MF vs. CON) and time (pre-post) in both balance tests, Eriksen-Flanker RT and spectral power, while paired sample t-tests were used to analyse the effect of condition on motivation and NASA-TLX subscales. We used a one-way ANOVA to analyse the differences on cognitive task performance; Stroop data were divided in eight identical time blocks and data sets were analysed separately for accuracy and reaction time for both colour (blue, green and yellow) and meaning (red).

For the brain imaging, we selected the same comparisons as for the spectral power analysis (condition and time during YBT and RBT), but performed t-statistics on log transformed exact low resolution brain electromagnetic tomography data. A critical t-value was determined, randomization (bootstrap with 5000 iterations) was completed, as well as the computation of critical thresholds and p values. A significant difference in a specific brain area can be considered when a voxel value exceeds the critical t value. In order to correct for the multiple comparisons, Statistical non-Parametric Mapping was used.

Results

Indicators of mental fatigue

For M-VAS, the RM ANOVA found an interaction effect of condition and time ($F(1.4, 14.1) = 5.785$, $p = 0.022$, $\eta^2 = 0.366$). Follow-up paired samples t-tests indicated that perceived mental fatigue was higher in MF compared to CON, both after the 90-min Stroop test ($p = 0.004$) as well as after the final balance session ($p = 0.048$). This was further confirmed by a time effect ($F(1.2, 6.1) = 10.343$, $p = 0.016$, $\eta^2 = 0.674$; see fig 2) that was only present in MF and not in CON. Pairwise comparisons showed that subjective mental fatigue post-intervention was higher compared to baseline ($p = 0.009$) and pre-intervention ($p = 0.004$). After the final balance session, mental fatigue was still higher compared to baseline ($p = 0.05$) and pre-intervention ($p = 0.031$), but was significantly lower compared to immediately after the intervention ($p = 0.003$).

Concerning the NASA-TLX, paired samples t-tests demonstrated that the mental demand ($p < 0.001$), temporal demand ($p = 0.002$), performance ($p = 0.016$) and effort ($p = 0.016$) subscales significantly increased in the mental fatigue condition, while the physical demand subscale did not significantly differ between conditions. The Wilcoxon signed ranked test showed a significant increase in the frustration subscale ($p = 0.002$) of the NASA-TLX in the mental fatigue condition. All data concerning the measuring scales can be found in Table 1. For the Eriksen-Flanker reaction time and accuracy no differences were found for time and condition (see Table 2). Also, the Stroop RT and ACC did not differ throughout the 90-min Stroop Colour Word Test for both the meaning and the colour stimuli (see Table 2).

Participants' intrinsic motivation and motivation for task success on the Matthews motivation scale did not differ between the MF and CON condition.

Table 1 – Measuring scale outcomes

Measuring scale (section)		MF	CON
Intrinsic motivation		18.3 ± 0.8	19.4 ± 1.4
Task success motivation		18.8 ± 1.7	16.4 ± 1.2
M-VAS	Baseline	25.2 ± 9.9	22.2 ± 6.8
	Pre 90-min task	27.2 ± 8.6	26.0 ± 7.9
	Post 90-min task	55.5 ± 8.5*^	23.5 ± 4.7
	Follow-up	44.5 ± 9.3*^	19.8 ± 4.4
NASA TLX – Mental demand		80.0 ± 2.9*	28.3 ± 6.9
NASA TLX – Physical demand		35.1 ± 10.95	13.3 ± 5.7
NASA TLX – Temporal demand		52.5 ± 8.2*	14.2 ± 5.9
NASA TLX - Performance		44.2 ± 4.9*	25.8 ± 5.4
NASA TLX – Effort		65.8 ± 4.2*	35.0 ± 11.6
NASA TLX - Frustration		60.1 ± 12.3*	27.5 ± 6.7

Data are presented as means ± SE.

* Significant difference between MF and CON ($P < 0.05$).

^ Significant difference between time point within the same condition ($P \leq 0.05$)

Table 2 – Stroop and flanker data

	VMRT (ms)		**ACC (%)**	
Stroop block - % completed	Blue-green-yellow (colour)	Red (meaning)	Blue-green-yellow (colour)	Red (meaning)
Block 1 – 12.5%	645.4 ± 29.8	731.0 ± 30.3	94.0 ± 0.2	88.6 ± 2.8
Block 2 – 25%	658.4 ± 32.0	720.1 ± 33.1	95.6 ± 0.9	90.8 ± 2.2
Block 3 – 37.5	659.3 ± 36.1	719.9 ± 36.4	94.8 ± 1.2	91.0 ± 1.7
Block 4 – 50%	664.1 ± 36.6	715.5 ± 35.6	92.5 ± 2.1	88.1 ± 2.7
Block 5 – 62.5%	660.6 ± 38.6	724.7 ± 36.3	90.3 ± 3.3	87.6 ± 5.5
Block 6 – 75%	649.7 ± 34.9	715.6 ± 28.8	91.3 ± 2.7	87.8 ± 3.5
Block 7 – 87.5%	635.5 ± 34.4	702.8 ± 26.9	89.8 ± 3.7	82.6 ± 4.7
Block 8 – 100%	637.9 ± 37.6	697.1 ± 32.5	90.2 ± 2.2	86.0 ± 5.5
Flanker Task -	**MF**		**CON**	
component	PRE	POST	PRE	POST
VMRT (ms)	376.2 ± 8.9	379.9 ± 13.8	370.1 ± 12.9	371.1 ± 11.2
ACC (%)	99.0 ± 0.5	96.3 ± 1.7	95.0 ± 0.9	93.5 ± 2.0

Data are presented as means ± SE. VMRT = visuomotor reaction time; ACC = accuracy

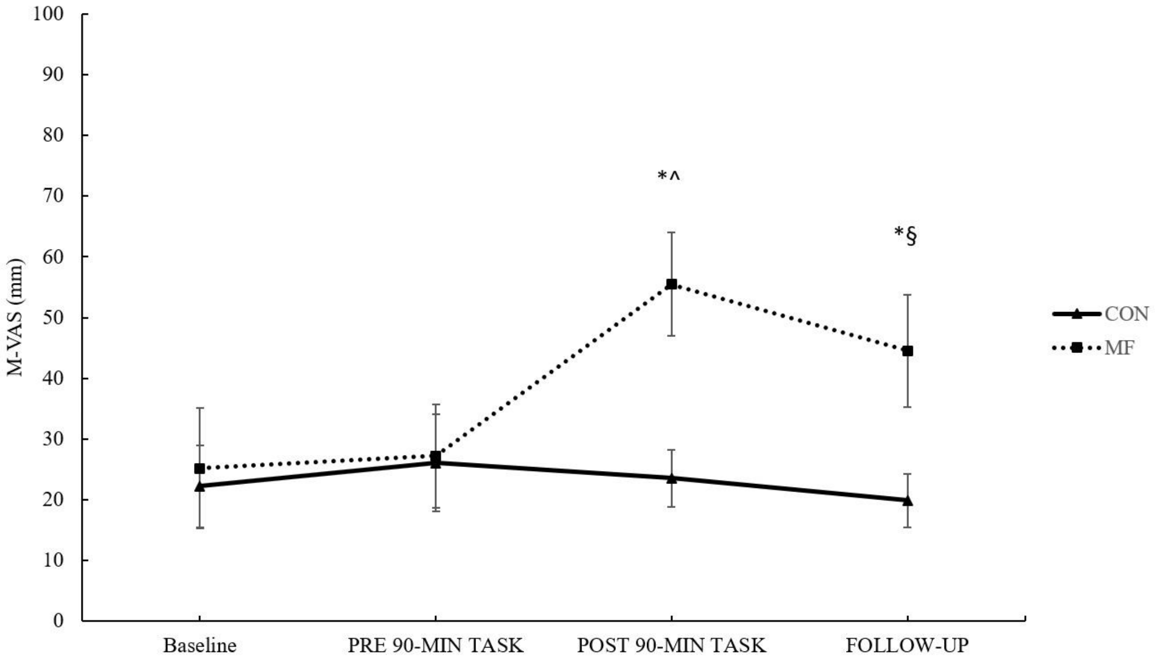

Figure 2 – Perceived mental fatigue (M-VAS). MF = Mental Fatigue group; CON = Control group.

* Significant difference between MF and CON ($P < 0.05$).

^ Significant higher MF in POST-intervention compared to baseline, PRE-intervention, and follow-up ($P \leq 0.01$)

§ Significantly higher MF in follow-up compared to baseline, and PRE-intervention

Balance performance (see Table 3)

No interaction effect between or main effects for condition and time were observed for YBT performance in the anterior, posteromedial and posterolateral direction, as well as for RBT VMRT. For the RBT accuracy, the RM ANOVA found a significant interaction effect between condition and time was present (F (1.0, 10.0) = 11.429, p = 0.007, $\eta^2 = 0.533$). Follow-up t-tests indicated no significant difference for RBT accuracy in both pre-conditions as well as between pre and post in CON. However, participants' RBT accuracy significantly decreased on the post-MF intervention compared to the pre-MF intervention (p = 0.001) and compared to post-CON (p = 0.044).

Table 3 – Balance outcomes

	MF		CON	
	PRE	POST	PRE	POST
YBT – ANT (cm)	64.5 ± 2.4	64.4 ± 1.9	62.2 ± 1.7	62.4 ± 1.4
YBT – PM (cm)	98.5 ± 2.9	99.6 ± 3.2	97.2 ± 3.7	98.7 ± 3.2
YBT – PL (cm)	98.3 ± 2.3	99.1 ± 2.3	96.3 ± 3.8	96.4 ± 2.9
RBT – VMRT (ms)	797.5 ± 39.7	732.5 ± 47.2	827.3 ± 49.2	803.4 ± 54.9
RBT – ACC (%)	90.4 ± 2.5	85.2 ± 1.9*^	90.0 ± 1.3	90.7 ± 2.2

Data are presented as means ± SE. VMRT = visuomotor reaction time; ACC = accuracy

* Significant difference between MF and CON (P = 0.044).

^ Significant difference between PRE and POST (P = 0.001)

Brain data

Spectral Power

For brain activity measured during YBT performance, we found a significant interaction effect between condition and time (F (1.0, 10.0) = 5.190; p = 0.046; $\eta^2 = 0.342$) of theta activity in the PFC. Post hoc t-tests revealed a significant increase in PFC theta activity during the post-YBT (0.09 ± 0.002 μV^2) compared to the pre-YBT (0.14 ± 0.03 μV^2) induced by MF (p = 0.04), but no differences were observed compared to the post-YBT in the control condition. Statistical analyses revealed no significant interaction or main effects for theta activity in the MC and PPC. In all other spectral power frequencies ($\alpha1$, $\alpha2$, $\beta1$, $\beta2$, and $\beta3$) across all regions of interest, no interaction or main effect of condition and time was detected. For brain activity measured during RBT performance no interaction or main effects of condition and time was observed in all spectral power frequencies (θ , $\alpha1$, $\alpha2$, $\beta1$, $\beta2$, and $\beta3$) across all regions of interest.

Brain imaging: source localisation

No differences in condition (MF vs. CON) or time (pre-post) were observed in all voxels across all band frequencies (θ , $\alpha1$, $\alpha2$, $\beta1$, $\beta2$, and $\beta3$) during both YBT and RBT performance.

Discussion

To the best of the authors' knowledge, this is the first study evaluating the interaction of mental fatigue with electrophysiological brain activity during YBT and RBT performance. Increases in M-VAS and NASA TLX following the 90-min Stroop Colour Word Test suggest that mental fatigue was successfully induced. Mental fatigue did not affect YBT performance, yet an increase in prefrontal cortex theta activity during the post-YBT performance was observed. The results further indicate that mental fatigue impairs the accuracy of RBT performance, while no changes in visuomotor reaction time and electrophysiological brain activity during post-RBT performance were found across all band frequencies and regions of interest.

Mental fatigue: successfully induced?

The M-VAS indicated that participants perceived higher levels of mental fatigue after the 90-min Stroop test and still after the second balance session compared to after the documentary. Also, the mental demand subscale of the NASA TLX demonstrated that participants required more attentional resources and perceived the Stroop test as more mentally demanding than watching a self-selected documentary. Nevertheless, no changes were observed in the cognitive task outcome measures (i.e. Stroop test, Eriksen Flanker test). Even though incongruent 90-min Stroop tests are an effective manner to induce mental fatigue, no significant differences were found for VMRT and ACC on the 90-min Stroop test over time, albeit a discernible trend showing participants progressively making more errors and reacting faster to the stimuli throughout the 90-min Stroop test [4,29]. Concerning the unchanged Eriksen Flanker test performance, our results are in line with previous research that did not observe changes in VMRT and ACC in Flanker task performance after 90-min cognitive tasks [2,4]. Further research is needed in order to better understand the role of VMRT and ACC as a hallmark of mental fatigue as well as its underlying mechanisms.

At the (electro)physiological level, the increased PFC theta activity could be an indicator of mental fatigue as it is in accordance with mental fatigue literature during exercise [6]. These changes in electrophysiological brain activity are assumed to clarify potential impairments in the allocation and availability of attentional resources, and provoke a decline in performance [2,4-8]. Important to take into account is that mental fatigue associated changes do not have to be present on all of the three levels (i.e. physiological, subjective and behavioural) to assert the presence of mental fatigue [1]. Given that in this study both changes at the subjective and physiological level arose, we concluded that mental fatigue was successfully induced.

Mental fatigue impairs RBT performance, but not YBT performance

The hypothesis concerning the deterioration of performance on both balance tests due to mental fatigue was partially substantiated by our results: Mental fatigue impaired RBT performance instigating a decline in the ACC component, while VMRT remained unaffected. YBT performance did not change as a consequence of mental fatigue or watching a documentary. Hachard and colleagues (2020) also assessed the effects of mental fatigue on balance control with a similar study design, but by using a more sensitive measuring instrument (i.e. force plate) [30]. They also let participants perform a 90-min continuous cognitive task (AX-continuous performance test) as an intervention and watch a 90-documentary as a control task, whereas balance control was measured before and after these 90-min tasks. Their results showed that both mental fatigue and watching a documentary impaired balance control in the three different quiet stance tasks. The authors mainly attributed their results to the deleterious effect of prolonged sitting rather than to impairments in cognitive or attentional resources [30]. For the YBT, one possible explanation might be that the sensitivity of the traditional YBT is insufficient to detect delicate changes in balance control. Even though the YBT is a clinician-friendly balance tests that is relied upon by practitioners, these results raise questions about the YBT's practical applicability in detecting subtle changes in balance control. Another potential explanation for our results might be that the more difficult (balance) tasks become, the more attentional resources are needed [4,31]. Mental fatigue would then not or mildly interfere with balance tests requiring a low level of attentional resources, and would be more likely to impair balance tests requiring a higher level of attentional resources. Applied to our study, it is hypothesized that the YBT requires less attentional resources in comparison with the RBT. This could explain why RBT performance was affected by mental fatigue and no differences were observed in the YBT. Yet, it would be unjustified to unilaterally attribute the effects of mental fatigue to underlying psychological mechanisms (i.e. attentional resources), and clarify or interpret them without the consideration of any physiological mechanisms.

Mental fatigue and electrophysiological brain activity during balance performance

The EEG analyses showed an increased PFC theta activity during post-YBT, but not in the MC or the PPC. No changes in alpha activity during post-YBT were observed after mental fatigue. These results were partly in line with the hypotheses that theta and alpha activity during post-YBT performance would increase as a consequence of mental fatigue. Despite the scarcity on the topic of mental fatigue and electrophysiological brain activity during balance performance, similar spectral power changes in electrophysiological PFC activity have been found during neurocognitive tasks after a prolonged cognitive task [2,5-8]. An increase in PFC theta and alpha activity are hypothesized to represent attentional deficits, impaired decision-making, and a reduced level of arousal [5,7,9,32]. The increase in PFC spectral power theta activity during the execution of the YBT could therefore also be related to a decrease in the availability of attention resources and impaired decision-making, yet at behavioural level YBT performance remained unaffected. Since the order of the YBT is predetermined and all movements being pre-planned, the YBT requires less continuous attention and decision-making in comparison to the RBT. This could explain why mental fatigue related changes at the physiological and psychological level did not translate to the behavioural level of YBT performance. One would expect to find similar or greater electrophysiological brain changes during post-RBT performance as a consequence of mental fatigue considering that the RBT requires a greater level of continuous attention and decision-making due to the addition of a neurocognitive task during this balance test. However, the results showed that mental fatigue did not increase theta or alpha activity during RBT performance across all three regions of interest. Even though the EEG results could not identify underlying physiological brain mechanisms that explain the observed decrement in RBT performance, future research should further explore mental fatigue related brain mechanisms. Nevertheless, the results of this study showed that mental fatigue was successfully induced at the physiological level and that it was possible to measure subtle electrophysiological brain activity changes during a complex balance task that approximates the clinical context.

Future directions

Further fundamental research is warranted to better understand the underlying physiological mechanisms that occur when mentally fatigued and interact with balance control and neurocognitive performance decrements. From the fundamental perspective, more sensitive balance measuring tools (i.e. force plate) could be utilized in order to get a better fundamental understanding of how mental fatigue interacts with balance control. This would also allow researchers to synchronize the EEG recording with these measuring instruments as well as with participants' movement initiation. This could prove to be an essential step to further explore potential electrophysiological mechanisms in relation to mental fatigue and human balance control. From the clinical perspective, future research should further try to bridge the gap between research and practice. For instance, mental fatigue research should be performed within the athletic context, since athletes tend to perceive mental fatigue to be an inhibiting factor in achieving their full potential and maximal performance. Slower neurocognitive performance, slower processing speed, and visuospatial disorientation have been associated with an increased lower extremity injury risk [17-19], suggesting a potential role for mental fatigue as an underlying mechanism in the occurrence of injuries. Future injury prevention research should examine the possible link between mental fatigue and injury risk, while also attempting to map potential underlying physiological mechanisms.

Perspective

MF impairs endurance performance, psychomotor skills, balance, neurocognitive performance and decision-making [1,2,4-8,10,11]. Alterations in neurocognitive performance have also been associated with an increased lower extremity injury risk [17-19] suggesting a potential role for MF as an underlying mechanism in the occurrence of injuries. The relevance to test and consider MF in a clinical (sport injury) context is further supported by the statement of athletes claiming to often encounter MF and it limiting their ability to perform optimally [21,22]. The findings of this study are in line with the above-mentioned MF related performance decrements. It might thus be of interest to clinicians that MF might be present during the execution of functional performance tests that are often used to compile injury risk profiles and to make return to sport decisions. The changes in brain activity during the YBT when mentally fatigued show that MF can be present during the execution of functional performance tests without clinicians being aware of it, given that YBT performance remained unchanged. Nevertheless, it is currently unknown which functional performance tests are affected by MF. Simple MF measuring scales and the use of neurocognitive functional performance tests, such as the RBT, might assist clinicians in detecting MF.

Conclusions

Mental fatigue can impair balance performance, and alters electrophysiological brain activity during balance performance. Mental fatigue induced a higher prefrontal cortex theta activity during the Y-balance test, without affecting Y-balance performance. In contrast, accuracy in the reactive balance test decreased when mentally fatigued, but no alterations in brain activity or visuomotor response time were observed in response to mental fatigue. Future studies should further explore the potential underlying brain mechanisms that coincide with mental fatigue and interfere with both balance and neurocognitive performance.

References

1. Van Cutsem J, Marcora S, De Pauw K, Bailey S, Meeusen R, Roelands B. The effects of mental fatigue on physical performance: a systematic review. Sports Med. 2017 Aug;47(8):1569-88.
2. Van Cutsem J, De Pauw K, Buyse L, Marcora S, Meeusen R, Roelands B. Effects of Mental Fatigue on Endurance Performance in the Heat. Medicine and Science in Sports and Exercise. 2017 Aug;49(8):1677-87.
3. Van Cutsem J, De Pauw K, Marcora S, Meeusen R, Roelands B. A caffeine-maltodextrin mouth rinse counters mental fatigue. Psychopharmacology (Berl). 2018 Apr;235(4):947-58.
4. Van Cutsem J, De Pauw K, Vandervaeren C, Marcora S, Meeusen R, Roelands B. Mental fatigue impairs visuomotor response time in badminton players and controls. Psychology of Sport and Exercise. 2019 2019/11/01/;45:101579.
5. Boksem MAS, Meijman TF, Lorist MM. Effects of mental fatigue on attention: an ERP study. Brain Res Cogn Brain Res. 2005;25(1):107-16.
6. Pires FO, Silva-Júnior FL, Brietzke C, Franco-Alvarenga PE, Pinheiro FA, de França NM, et al. Mental Fatigue Alters Cortical Activation and Psychological Responses, Impairing Performance in a Distance-Based Cycling Trial. Front Physiol. 2018;9:227-.
7. Wascher E, Rasch B, Sänger J, Hoffmann S, Schneider D, Rinkenauer G, et al. Frontal theta activity reflects distinct aspects of mental fatigue. Biological psychology. 2014;96:57-65.
8. Käthner I, Wriessnegger SC, Müller-Putz GR, Kübler A, Halder S. Effects of mental workload and fatigue on the P300, alpha and theta band power during operation of an ERP (P300) brain–computer interface. Biological Psychology. 2014 2014/10/01/;102:118-29.
9. Tops M, Boksem MA. Absorbed in the task: Personality measures predict engagement during task performance as tracked by error negativity and asymmetrical frontal activity. Cogn Affect Behav Neurosci. 2010 Dec;10(4):441-53.
10. Lew FL, Qu XD. Effects of mental fatigue on biomechanics of slips. Ergonomics. 2014 Dec;57(12):1927-32.
11. Qu X, Xie Y, Hu X, Zhang H. Effects of Fatigue on Balance Recovery From Unexpected Trips. Human factors. 2019:18720819858794-.
12. Wittenberg E, Thompson J, Nam CS, Franz JR. Neuroimaging of Human Balance Control: A Systematic Review. Frontiers in human neuroscience. 2017;11:170-.
13. Surgent OJ, Dadalko OI, Pickett KA, Travers BG. Balance and the brain: A review of structural brain correlates of postural balance and balance training in humans. Gait & posture. 2019 2019/06/01/;71:245-52.
14. Hartley EM, Hoch MC, Boling MC. Y-balance test performance and BMI are associated with ankle sprain injury in collegiate male athletes. Journal of science and medicine in sport. 2018 2018/07/01/;21(7):676-80.
15. Smith Ca, Chimera Nj, Warren M. Association of Y Balance Test Reach Asymmetry and Injury in Division I Athletes. Medicine & Science in Sports & Exercise. 2015;47(1):136-41.

16. Gonell AC, Romero JAP, Soler LM. Relationship between the y balance test scores and soft tissue injury incidence in a soccer team. Int J Sports Phys Ther. 2015;10(7):955-66.

17. Wilkerson GB, Mokha M. Neurocognitive reaction time predicts lower extremity sprains and strains. IJATT. 2012 Nov;17(6):4-9.

18. Swanik CB, Covassin T, Stearne DJ, Schatz P. The relationship between neurocognitive function and noncontact anterior cruciate ligament injuries. American Journal of Sports Medicine. 2007 Jun;35(6):943-8.

19. Herman DC, Barth JT. Drop-Jump Landing Varies With Baseline Neurocognition: Implications for Anterior Cruciate Ligament Injury Risk and Prevention. American Journal of Sports Medicine. 2016 Sep;44(9):2347-53.

20. Verschueren J, Tassignon B, Pluym B, Van Cutsem J, Verhagen E, Meeusen R. Bringing context to balance: development of a reactive balance test within the injury prevention and return to sport domain. Arch Physiother. 2019;9(6):eCollection 2019.

21. Russell S, Jenkins D, Rynne S, Halson SL, Kelly V. What is mental fatigue in elite sport? Perceptions from athletes and staff. European Journal of Sport Science. 2019;19(10):1367-76.

22. Russell S, Jenkins D, Smith M, Halsone S, Kelly V. The application of mental fatigue research to elite team sport performance: New perspectives. Journal of Science and Medicine in Sport. 2019 Jun;22(6):723-8.

23. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods. 2007 May;39(2):175-91.

24. Van Cutsem J, Roelands B, Pluym B, Tassignon B, Verschueren JO, De Pauw K, et al. Can Creatine Combat the Mental Fatigue-associated Decrease in Visuomotor Skills? Medicine and science in sports and exercise. 2020;52(1):120-30.

25. Matthews G, Campbell SE, Falconer S. Assessment of Motivational States in Performance Environments. Proc Hum Factors Ergon Soc Annu Meet. 2001;45(13):906-10.

26. Plisky PJ, Gorman PP, Butler RJ, Kiesel KB, Underwood FB, Elkins B. The reliability of an instrumented device for measuring components of the star excursion balance test. N Am J Sports Phys Ther. 2009 May;4(2):92-9.

27. Jasper HH. Report of the committee on methods of clinical examination in electroencephalography: 1957. Electroencephalogr Clin Neurophysiol. 1958 1958/05/01/;10(2):370-5.

28. Bear MF, Connors BW, Paradiso MA. Neuroscience: exploring the brain. Fourth ed: Wolters Kluwer; 2016.

29. Rozand V, Lebon F, Papaxanthis C, Lepers R. Effect of mental fatigue on speed-accuracy trade-off. Neuroscience. 2015;297:219-30.

30. Hachard B, Noé F, Ceyte H, Trajin B, Paillard T. Balance control is impaired by mental fatigue due to the fulfilment of a continuous cognitive task or by the watching of a documentary. Exp Brain Res. 2020 2020/03/07.

31. Lajoie Y, Teasdale N, Bard C, Fleury M. Attentional demands for static and dynamic equilibrium. Exp Brain Res. 1993 Dec;97(1):139-44.

32. Klimesch W. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res Brain Res Rev. 1999 Apr;29(2-3):169-95.

Chapter 5: Acute fatigue alters brain activity and impairs reactive balance test performance.

Bruno Tassignon

Jo Verschueren

Kevin De Pauw

Evert Verhagen

Romain Meeusen

Transl Sports Med (2021), published online while awaiting print

Abstract

Purpose

Conflicting results in Y-balance test (YBT) performance are found when participants are exposed to acute physical fatigue (APF). Even though APF is known to impair isolated neurocognitive performance, the effects of APF on reactive balance test (RBT) performance have never been investigated. Furthermore, research on the underlying APF induced neurophysiological mechanisms during these functional tests is scarce to non-existent. Therefore, the aim of this study was to assess the influence of APF on two clinician-friendly balance tests: the YBT and (RBT), as well as its effects on brain activity.

Methods

Twenty healthy adults (age = 24 ± 3 years) participated in this randomized counterbalanced cross-over study. APF was induced by a 30s modified Wingate test, while the time-matched control task encompassed sitting on the cycle ergometer. YBT performance was expressed in maximal reach distances, and RBT performance involved visuomotor reaction time and accuracy. Electroencephalography (EEG) was used to measure brain activity during these balance tests. Balance test performance and concurrent EEG recordings were analysed pre-post.

Results

APF was successfully induced given that heart rate, blood pressure, blood lactate concentration and rating of perceived exertion significantly increased following the modified Wingate. Decreased RBT accuracy was observed after APF, yet YBT performance and RBT visuomotor reaction time were unaffected. APF induced spectral power increments in the prefrontal cortex, motor cortex and posterior parietal cortex during both YBT and RBT performance.

Conclusion

Acute physical fatigue only impaired RBT performance, but did alter brain activity during both clinician-friendly balance tests.

Introduction

The Star Excursion Balance Test (SEBT) and Y-Balance Test (YBT) are commonly used in clinical practice to assess and identify injury risk in recreative and professional athletes [1,2]. Despite the merits of these clinician-friendly balance tests, they remain quite distant from the actual sports context. Recently, the reactive balance test (RBT) brought the YBT closer to the sports context by adding a neurocognitive task which involves environmental perception, decision-making and the selection of appropriate visuomotor responses while maintaining single leg balance [3]. In this perspective, the RBT might become a valuable addition to the clinician-friendly functional performance test repertoire, given that lower neurocognitive performance has been associated with an increased sport injury risk [4-6].

Another ubiquitous characteristic of the sport (injury) context is acute physical fatigue (APF). APF develops during, at the end or after exercise performance and emerges from a myriad of interactions between underlying peripheral and central physiological changes, individual psychological variables and the environment [7-10]. In sports science, APF is defined as a complex behavioural state resulting in exercise induced performance decrements [10]. In addition, APF is hypothesized to play a potential, yet controversial, role in the development and occurrence of sports injuries since a recent systematic review showed that APF can compromise intrinsic modifiable injury risk factors, such as proprioception, strength, and balance outcome measures [11]. When subjecting participants to different APF inducing protocols (e.g. high-intensity intermittent protocols, Wingate protocols), their SEBT and YBT reach distances worsen compared to a non-fatigued state [12-16]. While the RBT has never been exposed to similar APF protocols, neurocognitive components such as visuomotor response time and accuracy tend to deteriorate in consequence of APF [17-19]. Given these interactions between acute physical fatigue, injury risk and functional performance, a better understanding of the associated neurophysiological mechanisms is warranted to aid clinicians in interpreting these functional test outcomes. Nevertheless, research on potential underlying APF induced neurophysiological alterations during YBT, and neurocognitive performance impairments is scarce to non-existent.

Therefore, measuring the brain during YBT and RBT performance might prove valuable, given that the brain plays an essential role in the execution of neurocognitive tasks, the maintenance of balance and voluntary movement [20,21]. Currently, the majority of studies measuring electrophysiological brain activity during balance tasks are often limited to bipedal or single leg stance and stepping or walking tasks [21]. This implies that these results are difficult to translate and apply to specific clinician-friendly balance tests (i.e. YBT and RBT) utilized in clinical practice. The frontal-central-parietal brain regions are the most common brain areas researched in this domain due to their involvement in attention, spatial orientation, decision-making, predicting the outcome of actions, motor planning, and the control and execution of voluntary movements [21-24]. Interestingly, APF has also been shown to increase electrophysiological spectral power in similar brain areas during and after exercise-induced APF [25-27]. These findings lead to the hypotheses that similar APF induced electrophysiological brain alterations would occur during YBT and neurocognitive performance. Therefore, the aim of this study was to assess the influence of APF on two clinician-friendly balance tests: the YBT and RBT, as well as its effect on electrophysiological brain activity during these balance tests measured by means of electroencephalography (EEG).

Materials and methods

Participants, ethical approval and protocol registration

Twenty healthy recreationally trained individuals participated in this randomized, counterbalanced cross-over design. Participant characteristics can be found in Table 1. The sample size calculation for the effect of APF on YBT performance was based on previous research conducted by Ciliga et al. (2014) [28]. They found an effect size (ES) f value of 0.88, meaning that for repeated measures ANOVA with an alpha of 0.05 and power of 0.95, a sample size of 8 (with a 10% drop out rate: n = 9) would suffice in order to correctly interpret the results of the observed APF on functional performance. The power analyses for estimating the changes in EEG following APF was based on the review and meta-analyses of Crabbe et al. (2004) [26]. The mean ES for EEG alpha activity after an exercise bout was 0.54 (95% CI: 0.46 to 0.62), the mean ES for EEG beta activity after an exercise bout was 0.70 (95% CI 0.50 to 0.89). For repeated measures ANOVA with an alpha of 0.05 and power of 0.95, a sample size of 18 would suffice in order to correctly interpret the results of the observed APF effect on EEG measurements. We eventually included 20 participants to take a possible 10% drop out rate into account. Participants gave written informed consent and could ask further questions concerning the study. Participants were blinded for the fatigue hypotheses in order to reduce bias. Information about the fatigue hypotheses was provided immediately after the participant completed the final trial. Before the inclusion of each volunteer in the study, a medical examination by a medical doctor (LB) was conducted to clear participants for maximal effort or to exclude people with medical problems, using medication, or who had suffered a severe musculoskeletal injury in the past. The study was approved by the Medical Ethics Committee of the UZ Brussel of the Vrije Universiteit Brussel, Belgium (B.U.N. 143201939780). The study protocol and experimental procedures were registered and released on ClinicalTrials.gov Protocol Registration and Result System (NCT04030390).

Table 1 – Participant characteristics

Participant characteristic	
Age (mean ± SD)	24 ± 3 years
Height (mean ± SD)	1.8 ± 0.1 m
Weight (mean ± SD)	73.2 ± 11.3 kg
Sex (M/F)	8/12
Dominant hand: right (%)	100%
Dominant leg: right (%)	100%

M = number of male participants; F = number of female participants

Study protocol

Participants came to the lab three times. Each participant performed all trials in a neutral ambient temperature of 20°C, while each trial was planned at the same time of day with minimum one week between trials. The first trial for each participant was a familiarization trial and lasted about two hours. During the familiarisation trial, we gathered participants' characteristics (e.g. age, height, weight, head circumference for EEG cap), determined mean power output by means of a traditional Wingate protocol [29], and familiarized them with the questionnaires and measuring scales, the physiological monitoring equipment and procedures, EEG equipment and procedures, the YBT and RBT, and the actual maximal exercise task. -Participants performed a minimum of six practice trials for each balance test while wearing the EEG device in order to attenuate learning effects during the experimental and control trial. Another purpose of these six practice trials per test was to ensure that all participants were able to perform the YBT and RBT almost without additional movements causing artifacts in the EEG recordings. To achieve this, one member of the research team constantly checked whether the participant abided by the given instructions, while another researcher monitored the EEG recording on the computer. Since EEG recordings can be monitored in real-time, we were able to correct or adjust subjects when such artifacts or flatliners occurred. During these tests participants bend their knees so head movements are inherent to the task, but these occur in the delta frequency range, which lies beyond the frequency range of interest.

Figure 1 provides an overview of the experimental and control trial. The experimental and control trials lasted each 45 minutes and were identical except for the intervention (i.e. modified Wingate protocol) and the time-matched control task (i.e. sitting on cycle ergometer). The order of the experimental and control trials was randomized by means of a random number generator. Participants were instructed to refrain from (a) caffeinated and (b) alcohol containing products at least 1 day before and during each trial, (c) not perform any irregular physically exerting activities 24h before each trial, (d) sleep for at least 7 hours and (e) consume a similar meal before performing each trial. Participants had to complete a pre-trial checklist to confirm whether or not they followed these instructions. If a participant did not meet the abovementioned criteria, a new appointment was given. Participants always started the trials by filling in the pre-trial checklist and motivation scale. Subsequently, members of the research team collected blood at the earlobe to determine lactate concentration, measured participant's blood pressure, while the participant put on the heart rate monitor. Whilst applying the EEG cap on the participant's head and inserting the gel in the EEG electrodes, the members of research team repeated the specific instructions for optimal EEG recording during YBT and RBT performance. Before inserting the earplugs and starting the baseline EEG measurements, the YBT and RBT, the researchers always asked the participant to repeat the instructions out loud in order to confirm all instructions were clear. Next, we proceeded to the baseline EEG measurements. Participants then performed the first balance test session, starting with the YBT followed by the RBT. EEG was recorded during both balance tests. Immediately after the completion of the RBT, we collected blood lactate and blood pressure again. In the meantime participants were informed which task (modified Wingate or sitting) they had to carry out. During both the modified Wingate and time-matched control task, heart rate and rating of perceived exertion (RPE) were monitored at beginning and end of the warm-up (cycling or sitting), and at the end of the 30s experimental or control period. The moment participants completed the experimental or control task, all blood measures were gathered again as fast as possible in order to minimise time loss before starting the second balance session with EEG measurements. The second balance session was started within 2 ± 1 min and completed within 9 ± 1 min both after the modified Wingate and after the sitting task. Upon completion of the second balance test session, all blood measurements were collected one final time.

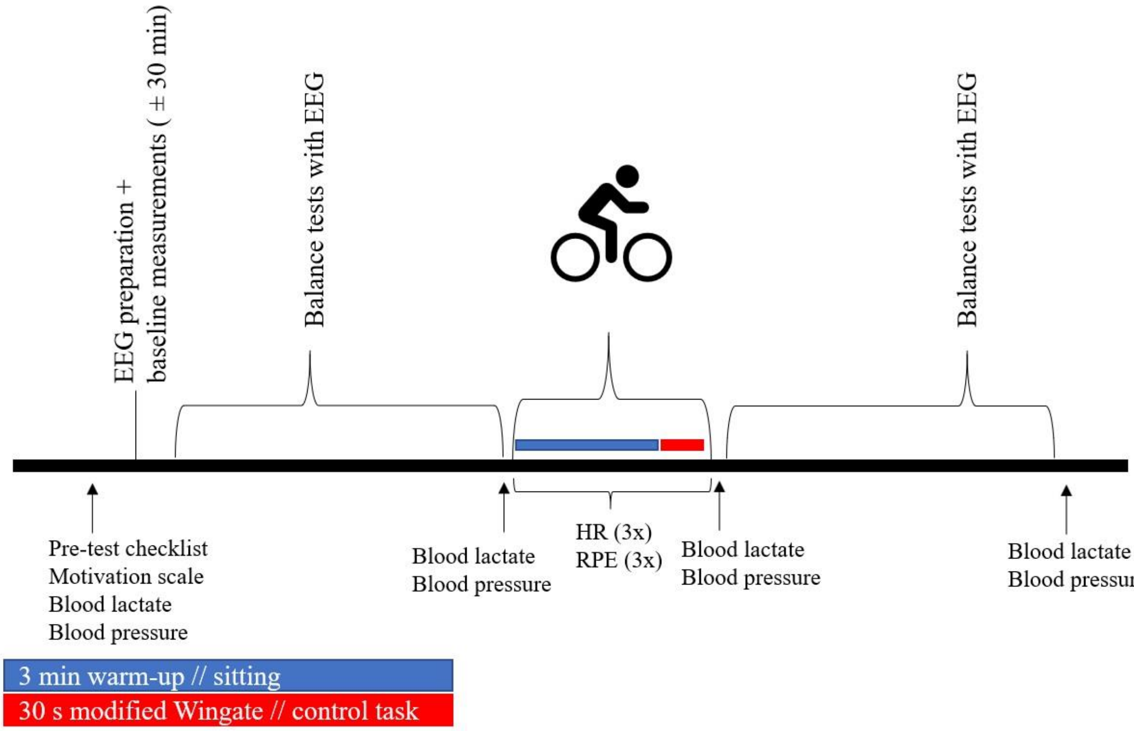

Figure 1 – Overview of study protocol. EEG = electroencephalography; HR= heart rate; RPE = rating of perceived exertion.

Acute physical fatigue protocol

Since post-exercise syncope commonly occurs in individuals after a traditional Wingate protocol [19,30], we extracted the mean power output and RPM of the 30 s all-out sprint for each participant. The traditional Wingate protocol was modified in order to decrease the possible occurrence of post-exercise syncope and to allow for swift transition to the post-balance test session. The modified Wingate protocol was performed on a cycle ergometer (Excalibur Sport, Lode, Groningen, The Netherlands). A 3 min warm-up at 80W between 60-80 RPM, was immediately followed by an individualised 30 s sprint effort with fixed resistance and target RPM. During the modified 30s sprint, the members of the research team encouraged participants in a standardized way to ensure maximal performance was reached.

Balance Tests

Y Balance test (YBT)

We used the Y-Balance Test Kit™ from Functional Movement Systems (FMS, Virginia, USA) and instructed participants to maximally push the three reach indicators along its axes (anterior, posteromedial, and posterolateral), while maintaining single leg balance. All instructions concerning the execution of the YBT were extracted from the study by Plisky et al. (2009) [31], and were complemented with the following instructions in order to minimize EEG movement artifacts: (1) to keep the hands on the pelvis [2] and (2) to keep the head and torso as stationary as possible. In order to help participants limit their head movement as much as possible during the YBT, the researchers placed a marking on the wall where the test subjects had to constantly look while performing the YBT. Outcome measure for each axis of the YBT was the maximal reach distance. In order to obtain reliable maximal reach distances and to have a sufficient amount of EEG recording time, participants performed the YBT four times (= 2 minutes equivalent) both at the beginning and at the end of the trial.

Reactive Balance test (RBT)

The goal of this test is to react as fast as possible to extinguish the correct axis-bound LED-light with your foot by passing over the light sensor of the LED-light while maintaining balance on the contralateral leg. The RBT consists of 4 LED-lights (Fitlights™, FITLIGHT Sports Corp., Aurora, Ontario, Canada): three are placed along the three axes of the Y-Balance Test Kit™ and one is placed in front of the YBT and serves as an indicator for the reach direction. Instructions and protocol were in accordance with Verschueren et al. (2019) [3]. A total of 45 stimuli were presented. To minimize EEG movement artifacts, identical instructions applied as during the YBT. In order to help participants limit their head movement as much as possible during the RBT, participants also had to constantly look at the indicator LED-light. The two main outcome measures of the RBT are accuracy (ACC) and visuomotor response time (VMRT). VMRT was automatically saved by computer software. For determining ACC, participants were filmed while performing the RBT in order to be able to perform a retrospective visual analysis of missed stimuli, multiple attempts and decision errors. We calculated ACC in accordance with the study of Verschueren et al. (2019) [3]. The ACC score was also taken into account for the correction of the VMRT outcomes.

Markers of acute physical fatigue

Systolic blood pressure was registered at the left arm by means of an electronic sphygmomanometer (Medisana AG, Neuss, Germany). We harvested capillary blood at the earlobe in order to determine blood lactate concentration (EKF; BIOSEN 5030, Magdeburg, Germany). During the modified Wingate protocol and sitting protocol, heart rate was continuously monitored by a heart rate monitor (Polar RS400, Polar Electro Oy, Kempele, Finland) and registered at three time points: during the warm up (1) after 30 seconds and after (2) 2min30s, and (3) right at the end of the 30s experimental or control task. The 15-points RPE scale (range: 6 to 20) was used to measure participants' perception of effort at the same three time points when heart rate was registered. Additionally, the motivation scale was filled in before each trial to assess intrinsic motivation and task motivation [32].

EEG recording and analysis

Brain activity was recorded during baseline measurements, the two YBTs and two RBTs. Baseline measures encompassed sitting 2 min with eyes closed and 2 min with eyes open followed by EEG recordings during YBT (2min) and RBT (2 min at least) performance. Thirty-two active Ag/AgCl electrodes were attached to the fitted EEG cap (actiCAP, Brain Products, Munich, Germany) in accordance with the "10–20 International System", and connected to the amplifier (BrainAMP DC, Brain Products, Munich, Germany). The sampling rate was set at 500 Hz (Brain Vision Recorder, Brain Products, Munich, Germany). Electrode impedance was kept below 10 kΩ throughout the recordings. During EEG recordings, participants inserted earplugs, and were instructed to minimize movement of the head and trunk, to avoid frowning, and to not touch their head in order to attenuate sound, muscle, electrode and cable movement artifacts, respectively.

Brain Vision Analyzer software (version 2.2) was used to (pre-)process the data sets. Raw data were re-referenced to an average reference and down-sampled to 256 Hz. Infinite Impulse Response Filters were set at 0.1 Hz (high pass), 45 Hz (low pass) and 48 dB/oct (Notch) with a Butterworth Zero Phase Filter design. Raw data inspection was carried out by means of manual artifact removal (i.e. electrode shifts, severe muscle artifacts). Next, Independent Component Analysis (Classic sphering, Extended Biased Infomax) allowed us to extract periodically recurring artifacts (i.e. eye and muscle artifacts) from the data. The scalp maps, time course of the components and the activity power spectrum were checked to determine whether the independent component was an artifact or brain-related. Scalp topography was accounted for channel noise, meaning that the independent component was removed from the dataset when the weighting was set on a single channel. Furthermore, the time course, matrix of weights and topographies were taken into account in order to remove bad components. The remaining good independent components were projected back to the original EEG signals.

Spectral power analysis

We extracted 4-s segments with an overlap of 1 s for each continuous EEG data set [33]. Fast Fourier transform (FFT) spectral power with a spectral resolution of 0.25 Hz was calculated for both sides of the spectrum for each segment. These FFT segments were averaged to determine the spectral content. The spectral power was exported for alpha (α1, 8–10 Hz; α2, 10.25–12.75 Hz), and beta (β1, 13–18 Hz; β2, 18.25–21 Hz; β3, 21.25–30 Hz) in each region of interest. The prefrontal cortex (PFC), motor cortex (MC) and posterior parietal cortex (PPC) were selected as regions of interest [21], because they play a vital role in dynamic balance and voluntary movement [20]: the prefrontal cortex (FP1, FP2, F3, Fz, F4), motor cortex (FC1, FC2, C3, Cz, C4) and posterior parietal cortex (CP1, CP2, P3, Pz, P4). The PFC is important for attention, decision-making, and predicting the outcome of actions; the MC is mainly involved in motor planning, and the control and execution of voluntary movements; the PPC is mostly engaged in spatial relations, attention, and motor planning [20].

EEG source localisation

In order to analyse the cortical distribution of current source density, we extracted 4-s segments with averaged data segments without overlap. Next, the data were exported to a .dat file to export the datasets into the program standardized low resolution brain electromagnetic tomography (LORETA^{KEY}) [34]. All procedures were in accordance with the open source LORETA manual concerning the analysis of EEG data. Information of the electrode positions were defined in a transformation matrix (.spinv) file. Each .txt file was converted to one cross spectrum (.crss) file and a standardized low resolution brain electromagnetic tomography (.slor) file for further statistical analysis.

Connectivity analyses

Connectivity analyses were performed by the computation of lagged linear (coherence) connectivity using the eLORETA algorithm in the LORETA^{KEY} software. Connectivity measures give an accurately corrected estimate of the statistical dependence between active sources for each pair of cortical ROIs within a specific frequency range. Therefore, it has been claimed that connectivity outcomes would mainly contain pure physiological information [35,36]. We estimated lagged linear connectivity for 3 ROIs (PFC, MC, PPC) defined by the LORETA^{KEY} software. All procedures were in accordance with the open source LORETA manual.

Statistical Analysis

The Statistical Package for the Social Sciences, version 26 (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. Significance was set at 0.05. Data are presented as mean values and standard error (SE) unless stated otherwise. Descriptive statistics were calculated, and data were tested for normal distribution using the Shapiro-Wilk test and visual interpretation of histograms. If data were not normally distributed, data were transformed using square root transformation (i.e. RBT accuracy, RBT VMRT, RPE, overall YBT and RBT spectral power data). When transformed data were not normally distributed after transformation (i.e. RPE, overall $\alpha1_{YBT}$, overall $\alpha2_{YBT}$, PFC $\beta1_{YBT}$, MC $\beta2_{YBT}$, overall $\alpha1_{RBT}$), the original data were analysed by means of Wilcoxon signed rank tests. When data were normally distributed, parametric testing commenced with a repeated measures analysis of variance (RM ANOVA). Sphericity was verified by the Mauchly's test, and significance and F-ratios were evaluated. When the assumption of sphericity was not met ($\varepsilon < 0.75$), RM ANOVA outcomes were interpreted according to the Greenhouse-Geisser procedure.

If RM ANOVA outcomes identified a significant interaction effect of condition (acute physical fatigue) and time, subsequent two-way RM ANOVA analyses or post hoc paired t-tests were used to evaluate the pairwise differences of condition and time. When RM ANOVA did not show a significant interaction effect, the main effects of condition and time were interpreted.

For the EEG source localisation, the same comparisons as for the spectral power analysis were selected but we performed t-statistics on log transformed exact low-resolution brain electromagnetic tomography data. For the connectivity analyses identical comparisons were carried out by using t-statistics. For both the EEG source localisation and connectivity analyses, a critical t-value was determined, randomization (bootstrap with 5000 iterations) was completed, as well as the computation of critical thresholds and p values with the LORETA$^{\text{KEY}}$ software. In order to correct for the multiple comparisons in both the source localisation as the connectivity analyses, Statistical non-Parametric Mapping was used in the LORETA$^{\text{KEY}}$ software.

Results

Markers of acute physical fatigue

Table 2 gives an overview of these markers and states the significant statistical differences. These results indicate that APF was induced due to the modified Wingate protocol. The mean power output during the 30 s modified Wingate sprint was 98.4 ± 0.6 % percent compared to the mean power output of the traditional Wingate protocol. Maximal effort was further confirmed, since visual inspection of the RPM data during the 30s Modified Wingate showed that all participants could not maintain their target RPM during the last 5 seconds of this test. No significant differences were observed in intrinsic motivation and perception of task success in the control and fatigue intervention.

Table 2 - Markers of acute physical fatigue

Marker	Time point	FATIGUE	CONTROL
Intrinsic motivation	Baseline	21.9 ± 0.8	21.8 ± 0.7
Perception of task success	Baseline	18.6 ± 1.1	18.5 ± 1.0
Heart rate (bpm)	Warm-up at 30s	116.2 ± 4.2*	75.2 ± 2.5
	Warm-up at 2min30s	122.8 ± 4.8*^	74.9 ± 2.8
	End 30s task	174.2 ± 2.6*^	75.4 ± 2.7
Rating of perceived exertion	Warm-up at 30s	8.2 ± 0.4*	6.2 ± 0.1
	Warm-up at 2min30s	9.3 ± 0.5*^	6.2 ± 0.1
	End 30s task	17.9 ± 0.3*^	6.2 ± 0.1
Systolic blood pressure (mmHg)	Baseline	125.6 ± 2.4	121.6 ± 1.8
	Pre-fatigue/CON	126.1 ± 2.6	129.7 ± 3.0
	Post-fatigue/CON	169.8 ± 8.1*^	125.6 ± 3.3
	Post-balance session 2	129.3 ± 3.1§	124.6 ± 3.4
Blood lactate (mmol/L)	Baseline	1.2 ± 0.1	1.2 ± 0.1
	Pre-fatigue/CON	1.1 ± 0.1	1.2 ± 0.1
	Post-fatigue/CON	5.2 ± 0.3*^	1.1 ± 0.1
	Post-balance session 2	7.1 ± 0.3*^	1.2 ± 0.1

* Significant difference between the fatigue condition and the control condition.

^ Significant increase in comparison to previous time points.

§ Significant decrease in comparison to previous time point.

Balance tests

Table 3 shows the results of both the YBT and RBT. RBT accuracy worsened after APF compared to before ($p = 0.004$). Also, RBT accuracy was lower after the modified Wingate compared to the sitting task ($p < 0.001$). APF did not affect RBT VMRT and YBT reach distances. However, a main effect of time was observed for RBT VMRT ($p = 0.023$) and all YBT reach directions ($p < 0.05$), as well as main effect of condition for the anterior reach direction ($p = 0.04$).

Table 3 – Balance test outcomes

	FATIGUE		CONTROL	
Outcome	PRE	POST	PRE	POST
YBT – ANT (cm) § °	58.0 ± 1.2	58.6 ± 1.0	58.5 ± 1.3	60.3 ± 1.1
YBT – PM (cm) §	91.0 ± 2.0	93.4 ± 1.9	91.3 ± 2.2	93.8 ± 1.9
YBT – PL (cm) §	85.1 ± 2.2	87.4 ± 2.3	86.8 ± 2.4	89.2 ± 2.0
RBT – VMRT (ms) §	767.6 ± 54.8	762.8 ± 55.8	798.1 ± 62.6	758.5 ± 57.7
RBT – ACC (%)	87.6 ± 2.0	81.2 ± 2.7*^	90.2 ± 1.2	89.9 ± 1.4

YBT = Y-balance test; ANT = anterior reach distance; PM = posteromedial reach distance; PL = posterolateral reach distance; RBT = reactive balance test; VMRT = visuomotor response time; ACC = accuracy.

* Significant difference between the fatigue condition and the control condition.

^ Significant difference between PRE and POST.

§ Significant main effect of time.

° Significant main effect of condition.

Brain data

All EEG recordings were successful and were included in the data analysis for each participant.

Spectral Power analyses

Tables 4 and 5 provide an overview of the spectral power data during YBT and RBT performance, respectively. During YBT performance, APF induced overall higher PFC spectral power across all band frequencies, except for the α1 frequency range. Higher cortical activity in the MC was observed in the α2 and β2 band frequencies as a consequence of APF, while APF also induced α2, β1 and β2 increments in the PPC.

During RBT performance, a significant increase in PFC β3 activity occurred after the modified Wingate compared to before the cycling task. PFC β3 activity was also significantly lower before the fatiguing task in comparison to before the sitting task. For PPC α1 activity, a significant increased cortical activity was registered after the APF inducing task compared to the pre-condition.

EEG source localisation

No differences in condition (APF vs. CON) or time (pre-post) during both YBT and RBT performance were observed in all voxels across all band frequencies (α1, α2, β1, β2, and β3).

Connectivity analyses

During YBT execution, no differences in condition (APF vs. CON) or time (pre-post) were identified in connectivity across all band frequencies (α1, α2, β1, β2, and β3).

During RBT execution, lagged linear connectivity increased in the β1 frequency band between MC and PFC during the RBT in a fatigued state (see fig 2 – a; t_{max} = 3.115). Lagged linear connectivity also increased in the β1 frequency band between MC and PPC during the RBT after the APF inducing task compared to the RBT after the control sitting task (see fig 2 – b; t_{max} = 3.065). No other differences in condition (APF vs. CON) or time (pre-post) during RBT execution were observed in connectivity across all other band frequencies (α1, α2, β2, and β3).

Table 4 – Spectral power data during YBT

Region of interest	Frequency band	FATIGUE PRE (μV²)	FATIGUE POST (μV²)	CONTROL PRE (μV²)	CONTROL POST (μV²)
Prefrontal cortex	α1	.078 ± .010	.086 ± .014	.068 ± .008	.070 ± .008
	α2	.062 ± .009	**.106 ± .018*^**	.074 ± .015	.069 ± .008
	β1	.035 ± .003	**.046 ± .006^**	.033 ± .003	.036 ± .002
	β2	.032 ± .003	**.048 ± .005*^**	.039 ± .006	.034 ± .003
	β3	.025 ± .003	**.038 ± .005*^**	.028 ± .004	.027 ± .003
Motor cortex	α1	.060 ± .006	.091 ± .018	.066 ± .010	.063 ± .008
	α2	.057 ± .009	**.092 ± .016*^**	.058 ± .011	.059 ± .008
	β1§	.025 ± .002	.034 ± .003	.023 ± .002	.029 ± .003
	β2	.020 ± .002	**.027 ± .003*^**	.022 ± .004	.023 ± .002
	β3§	.015 ± .002	.018 ± .001	.014 ± .001	.016 ± .002
Posterior parietal cortex	α1	.100 ± .020	.105 ± .021	.070 ± .011	.079 ± .013
	α2	.087 ± .020	**.136 ± .035*^**	.081 ± .016	.081 ± .012
	β1	.031 ± .003	**.045 ± .006*^**	.027 ± .003	.030 ± .003
	β2	.019 ± .002	**.031 ± .003*^**	.020 ± .002	.019 ± .001
	β3§ °	.013 ± .001	.016 ± .001	.012 ± .001	.013 ± .001

* Significant difference between the fatigue condition and the control condition.

^ Significant difference between PRE and POST.

§ Significant main effect of time.

° Significant main effect of condition.

Table 5 – Spectral power data during RBT

Region of interest	Frequency band	FATIGUE		CONTROL	
		PRE (μV^2)	POST (μV^2)	PRE (μV^2)	POST (μV^2)
Prefrontal cortex	α1	.097 ± .014	.102 ± .016	.093 ± .007	.091 ± .010
	α2	.085 ± .015	.080 ± .010	.076 ± .010	.078 ± .010
	β1	.049 ± .007	.047 ± .004	.048 ± .005	.047 ± .006
	β2	.039 ± .006	.046 ± .007	.048 ± .008	.044 ± .007
	β3	**.026 ± .003***	**.035 ± .005^**	.036 ± .006	.030 ± .004
Motor cortex	α1	.073 ± .013	.089 ± .014	.077 ± .011	.089 ± .011
	α2	.058 ± .009	.067 ± .011	.061 ± .008	.060 ± .009
	β1	.031 ± .004	.031 ± .003	.033 ± .004	.033 ± .003
	β2	.024 ± .003	.027 ± .003	.024 ± .003	.029 ± .004
	β3§	.015 ± .002	.018 ± .002	.016 ± .002	.020 ± .002
Posterior parietal cortex	α1	.093 ± .012	**.119 ± .017^**	.095 ± .009	.091 ± .014
	α2	.099 ± .021	.104 ± .018	.077 ± .011	.083 ± .013
	β1	.034 ± .003	.037 ± .004	.029 ± .003	.035 ± .005
	β2§	.021 ± .002	.027 ± .003	.020 ± .002	.026 ± .003
	β3§	.014 ± .001	.017 ± .001	.014 ± .001	.016 ± .002

* Significant difference between the fatigue condition and the control condition.

^ Significant difference between PRE and POST;

§ Significant main effect of time.

° Significant main effect of condition.

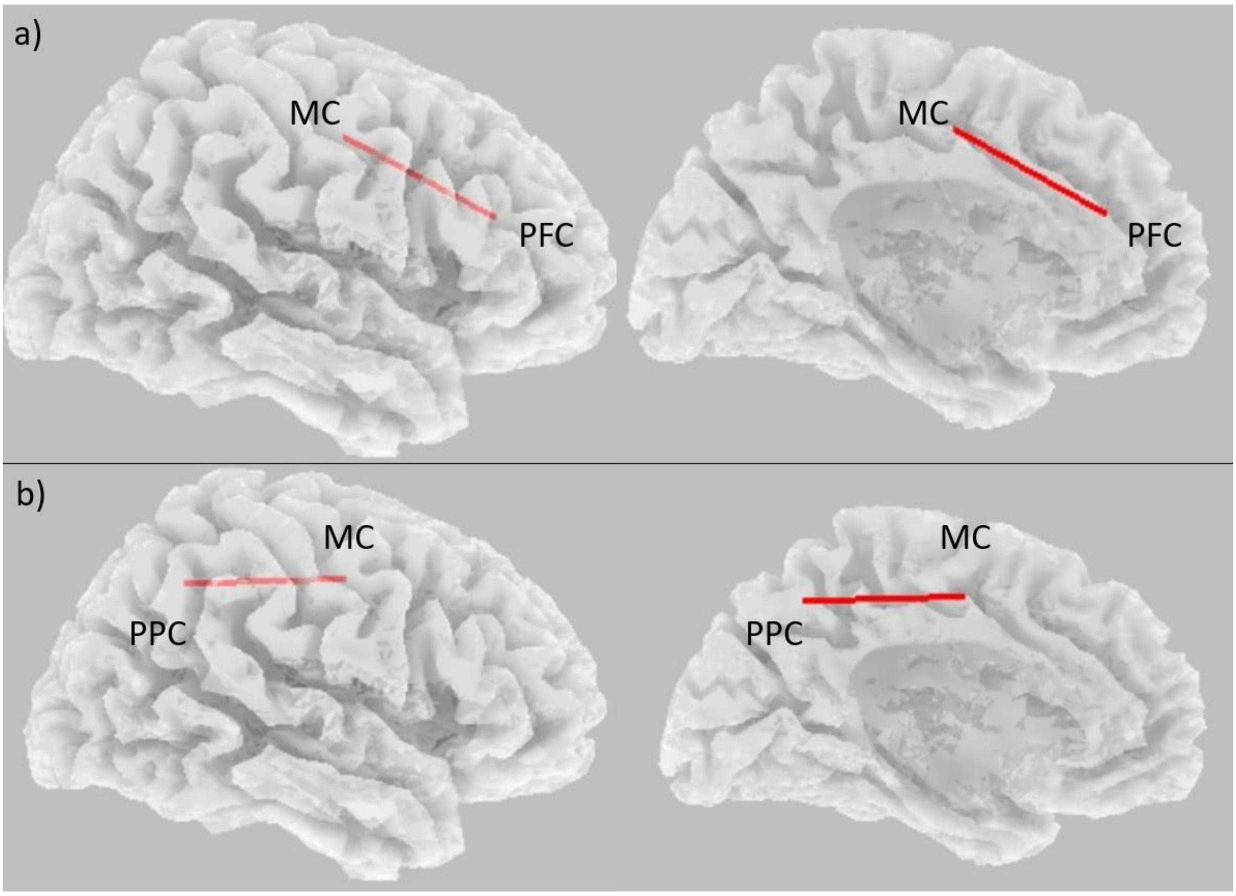

Figure 2 – a: (right view) – eLORETA wire diagram indicating PFC and MC with significantly increased β1 lagged linear connectivity during post-RBT execution in a fatigued stated compared to pre-RBT execution**. b:** (right view) – eLORETA wire diagram indicating MC and PPC with significantly increased β1 lagged linear connectivity during post-RBT execution in a fatigued stated compared to post-RBT execution in the control condition.

Discussion

To the best of the authors' knowledge, this is the first study assessing the interaction of acute physical fatigue with electrophysiological brain activity during YBT and RBT performance. All markers of APF indicated that the modified Wingate protocol successfully induced APF. Participants' RBT accuracy deteriorated due to APF and VMRT remained unaffected, while YBT performance slightly improved over time regardless of condition. Furthermore, a considerable amount of cortical activity changes were induced due to APF, although these cortical activity changes were more prominent during YBT performance than during RBT performance.

Acute physical fatigue and balance test performance

During the second execution of the YBT, the results showed a main effect of time for all three reach directions with participants reaching on average 1 to 2.5 cm further. This is in contrast to the findings of Johnston and colleagues (2018), who reported that reach distances in all three directions of the YBT deteriorated after a 60s modified Wingate test [16]. The main discrepancies can probably be explained by the difference in applied Wingate protocols. When comparing the reported markers of APF, only mean HR immediately after both Wingate performances was available for comparison. Mean HR immediately after the Wingate protocol was 10 bpm lower in our study compared to the results of Johnston and colleagues (2018). In addition, contrasting results in SEBT performance have been found between studies using more sport-specific and longer fatiguing protocols [12,14,15,37]. Another factor potentially influencing YBT performance are the instructions to keep the hands on the pelvis during the execution of this test. Although the YBT is reliable with both instructions, free moving hands during YBT lead to significant greater maximal reach distances in the posteromedial and -lateral directions 38 This could also possibly explain why we did not observe any differences in YBT performance following APF. Nevertheless, Johnston and colleagues (2018) let participants carry out the YBT with their hands on the pelvis and found major decreases in YBT performance in all three reach directions. [16] We therefore postulate that the differences in fatigue protocols might be the biggest underlying factor to clarify these contrasting YBT and SEBT results.

In terms of RBT performance, APF negatively affected the accuracy of participants without impairing visuomotor response time. Even though the RBT has never been exposed to similar or different APF protocols, this decline in accuracy is in line with research assessing the influence of APF on neurocognitive outcomes [17-19]. Underlying peripheral and central mechanisms are suggested to contribute to the degradation of performance after a traditional Wingate protocol, with central mechanisms being hypothesized as the main driver [38]. In this study, these peripheral and central mechanisms are likely be responsible for the impairment in RBT performance.

Acute physical fatigue and brain activity during YBT and RBT performance

The results demonstrate that the brain functions differently after APF while performing these clinician-friendly balance tests. Increased α and β power following APF are in line with previous literature, and may suggest the recruitment of previously uninvolved neurons and increased cognitive processing [25-27]. Yet, interpretations should be made prudently regarding APF induced spectral power changes, since these changes can comprehend both various physiological (e.g. biochemical, metabolic) and psychological (e.g. cognitive, emotional) alterations [27]. Even though APF did not affect YBT performance, a myriad of α and β power increments occurred across the PFC, MC and PPC during YBT performance after the modified Wingate. This could suggest that participants were able to overcome both peripheral and central APF induced changes in order to maintain their YBT performance. Nevertheless, these APF induced changes resulted in participants obtaining a lower accuracy during RBT performance. In the fatigued state, higher PPC α1 activity during RBT performance was induced in comparison to before the fatiguing task. Alpha oscillations play an active role in cognitive processing and self-regulation and might suggest greater cognitive processing requirements during RBT following APF [39]. Concurrently, PFC β3 activity during RBT performance increased due to APF suggesting higher cortical activation and higher attentional demand[27]. Additionally, elevated β1 connectivity between PFC and MC as well as between PPC and MC during the post-APF RBT performance could further contribute to this interpretation. However, the current study design and analyses do not allow to interpret the observed changes in the brain and the change in performance in terms of causality. This would require future research to conduct studies with a larger sample size and more sensitive analyses (e.g., mediation analysis, change-change analysis). Therefore future research should explore APF related brain mechanisms and the role they play in affecting functional performance tests. The take home messages for clinicians are that brain activity during YBT and RBT performance in a non-fatigued is different, with more baseline cortical activity present when participants performed the RBT. This could be explained by the continuous nature of the RBT as well as the added neurocognitive task that warrants environmental perception and decision-making in comparison to the pre-planned execution of the YBT. Due to the underlying differences in theoretical constructs, outcome measures, brain activity and sensitivity to fatigue between the YBT and RBT, clinicians could regard these tests as complementary. Nevertheless, further research is warranted in order to investigate the added value of the RBT in clinical practice. Furthermore, clinicians should be aware that APF did not affect YBT performance or RBT visuomotor reaction time, but did impair RBT accuracy. Additionally, APF altered brain activity during both YBT and RBT performance. The observation that different brain changes occurred during the YBT and RBT in response to APF, highlight the distinction but potential complementary nature of the YBT and RBT.

Perspective

Alterations in neurocognitive performance have been associated with an increased lower extremity injury risk [4-6] suggesting a potential role for APF as an underlying mechanism in the occurrence of injuries. It might thus be of interest to clinicians that APF might be present during the execution of functional performance tests that are often used to compile injury risk profiles and to make return to sport decisions. The changes in brain activity during YBT performance when physically fatigued show that APF can be present during the execution of functional performance tests without clinicians being aware of it, given that YBT performance remained unchanged. Nevertheless, it is currently not entirely clear which functional performance tests are affected by APF. Simple APF measuring scales and the use of neurocognitive functional performance tests, such as the RBT, might assist clinicians in detecting APF.

Conclusions

Acute physical fatigue impairs accuracy in the RBT while visuomotor reaction time and YBT performance remained unaffected. During the execution of both balance tests, acute physical fatigue induced alterations in brain activity. More specifically, during the execution of the YBT, acute physical fatigue induced higher α activity in the prefrontal cortex, motor cortex and posterior parietal cortex as well as higher β activity in the prefrontal and posterior parietal cortex. During RBT performance in a fatigued state, α and β power increments were observed in the posterior parietal cortex and the prefrontal cortex, respectively. Furthermore, acute physical fatigue affected connectivity between the prefrontal cortex and motor cortex as well as the motor cortex and posterior parietal cortex in the β band frequency during RBT execution.

References

1. Hegedus EJ, McDonough SM, Bleakley C, Baxter D, Cook CE. Clinician-friendly lower extremity physical performance tests in athletes: a systematic review of measurement properties and correlation with injury. Part 2-the tests for the hip, thigh, foot and ankle including the star excursion balance test. *Br J Sports Med.* 2015;49(10):649-656.
2. Gribble PA, Hertel J, Plisky P. Using the star excursion balance test to assess dynamic postural-control deficits and outcomes in lower extremity injury: a literature and systematic review. *J Athl Train.* 2012;47(3):339-357.
3. Verschueren J, Tassignon B, Pluym B, Van Cutsem J, Verhagen E, Meeusen R. Bringing context to balance: development of a reactive balance test within the injury prevention and return to sport domain. *Arch Physiother.* 2019;9(6):eCollection 2019.
4. Wilkerson GB, Mokha M. Neurocognitive reaction time predicts lower extremity sprains and strains. *IJATT.* 2012;17(6):4-9.
5. Swanik CB, Covassin T, Stearne DJ, Schatz P. The relationship between neurocognitive function and noncontact anterior cruciate ligament injuries. *American Journal of Sports Medicine.* 2007;35(6):943-948.
6. Herman DC, Barth JT. Drop-Jump Landing Varies With Baseline Neurocognition: Implications for Anterior Cruciate Ligament Injury Risk and Prevention. *American Journal of Sports Medicine.* 2016;44(9):2347-2353.
7. Marcora SM. Do we really need a central governor to explain brain regulation of exercise performance? *European Journal of Applied Physiology.* 2008;104(5):929-931.
8. Meeusen R, Roelands B. Fatigue: Is it all neurochemistry? *European Journal of Sport Science.* 2018;18(1):37-46.
9. Taylor JL, Amann M, Duchateau J, Meeusen R, Rice CL. Neural Contributions to Muscle Fatigue: From the Brain to the Muscle and Back Again. *Medicine and Science in Sports and Exercise.* 2016;48(11):2294-2306.
10. Knicker AJ, Renshaw I, Oldham ARH, Cairns SP. Interactive processes link the multiple symptoms of fatigue in sport competition. *Sports Med.* 2011;41(4):307-328.
11. Verschueren J, Tassignon B, De Pauw K, et al. Does Acute Fatigue Negatively Affect Intrinsic Risk Factors of the Lower Extremity Injury Risk Profile? A Systematic and Critical Review. *Sports Med.* 2020;50(4):767-784.
12. Baghbani F, Woodhouse LJ, Gaeini AA. Dynamic postural control in female athletes and nonathletes after a whole-body fatigue protocol. *Journal of Strength and Conditioning Research.* 2016;30(7):1942-1947.
13. McMullen KL, Cosby NL, Hertel J, Ingersoll CD, Hart JM. Lower Extremity Neuromuscular Control Immediately After Fatiguing Hip-Abduction Exercise. *Journal of Athletic Training.* 2011;46(6):607-614.

14. Zech A, Steib S, Hentschke C, Eckhardt H, Pfeifer K. Effects of localized and general fatigue on static and dynamic postural control in male team handball athletes. *J Strength Cond Res.* 2012;26(4):1162-1168.
15. Whyte E, Burke A, White E, Moran K. A high-intensity, intermittent exercise protocol and dynamic postural control in men and women. *J Athl Train.* 2015;50(4):392-399.
16. Johnston W, Dolan K, Reid N, Coughlan GF, Caulfield B. Investigating the effects of maximal anaerobic fatigue on dynamic postural control using the Y-Balance Test. *J Sci Med Sport.* 2018;21(1):103-108.
17. Whyte EF, Gibbons N, Kerr G, Moran KA. Effect of a High-Intensity, Intermittent-Exercise Protocol on Neurocognitive Function in Healthy Adults: Implications for Return-to-Play Management After Sport-Related Concussion. *J Sport Rehabil.* 2015;24(4).
18. Pavelka R, Třebický V, Třebická Fialová J, et al. Acute fatigue affects reaction times and reaction consistency in Mixed Martial Arts fighters. *PloS one.* 2020;15(1):e0227675.
19. Sieck DC, Ely MR, Romero SA, Luttrell MJ, Abdala PM, Halliwill JR. Post-exercise syncope: Wingate syncope test and visual-cognitive function. *Physiol Rep.* 2016;4(16).
20. Bear MF, Connors BW, Paradiso MA. *Neuroscience: exploring the brain.* Fourth ed: Wolters Kluwer; 2016.
21. Wittenberg E, Thompson J, Nam CS, Franz JR. Neuroimaging of Human Balance Control: A Systematic Review. *Frontiers in human neuroscience.* 2017;11:170-170.
22. Edwards AE, Guven O, Furman MD, Arshad Q, Bronstein AM. Electroencephalographic Correlates of Continuous Postural Tasks of Increasing Difficulty. *Neuroscience.* 2018;395:35-48.
23. Goel R, Nakagome S, Rao N, Paloski WH, Contreras-Vidal JL, Parikh PJ. Fronto-Parietal Brain Areas Contribute to the Online Control of Posture during a Continuous Balance Task. *Neuroscience.* 2019;413:135-153.
24. Varghese JP, McIlroy RE, Barnett-Cowan M. Perturbation-evoked potentials: Significance and application in balance control research. *Neuroscience and Biobehavioral Reviews.* 2017;83:267-280.
25. Enders H, Cortese F, Maurer C, Baltich J, Protzner AB, Nigg BM. Changes in cortical activity measured with EEG during a high-intensity cycling exercise. *J Neurophysiol.* 2016;115(1):379-388.
26. Crabbe JB, Dishman RK. Brain electrocortical activity during and after exercise: A quantitative synthesis. *Psychophysiology.* 2004;41(4):563-574.
27. Moraes H, Ferreira C, Deslandes A, et al. Beta and alpha electroencephalographic activity changes after acute exercise. *Arquivos de Neuro-Psiquiatria.* 2007;65:637-641.
28. Ciliga D, Bobic TT, Filipovic B. Effect of fatigue on dynamic balance in different directions. *Fundamental and Applied Kinesiology – Steps Forward.* 2014(7th International Scientific Conference on Kinesiology):27-30.
29. Inbar O, Bar-Or O, Skinner JS. *The Wingate anaerobic test.* Champaign (Ill.): Human Kinetics; 1996.
30. Lacewell AN, Buck TM, Romero SA, Halliwill JR. Postexercise syncope: Wingate syncope test and effective countermeasure. *Experimental physiology.* 2014;99(1):172-186.

31. Plisky PJ, Gorman PP, Butler RJ, Kiesel KB, Underwood FB, Elkins B. The reliability of an instrumented device for measuring components of the star excursion balance test. *N Am J Sports Phys Ther.* 2009;4(2):92-99.
32. Matthews G, Campbell SE, Falconer S. Assessment of Motivational States in Performance Environments. *Proc Hum Factors Ergon Soc Annu Meet.* 2001;45(13):906-910.
33. Van Cutsem J, De Pauw K, Marcora S, Meeusen R, Roelands B. A caffeine-maltodextrin mouth rinse counters mental fatigue. *Psychopharmacology (Berl).* 2018;235(4):947-958.
34. Pascual-Marqui RD, Michel CM, Lehmann D. Low-resolution electromagnetic tomography - a new method for localizing electrical-activity in the brain. *International Journal of Psychophysiology.* 1994;18(1):49-65.
35. Pascual-Marqui RD. Instantaneous and lagged measurements of linear and nonlinear dependence between groups of multivariate time series: frequency decomposition. *arXiv.* 2007:arXiv:0711.1455.
36. Pascual-Marqui RD, Lehmann D, Koukkou M, et al. Assessing interactions in the brain with exact low-resolution electromagnetic tomography. *Phil Trans R Soc A.* 2011;369:3768–3784.
37. Armstrong R, Brogden CM, Milner D, Norris D, Greig M. The Influence of Fatigue on Star Excursion Balance Test Performance in Dancers. *Journal of Dance Medicine & Science.* 2018;22(3):142-147.
38. Fernandez-del-Olmo M, Rodriguez FA, Marquez G, et al. Isometric knee extensor fatigue following a Wingate test: peripheral and central mechanisms. *Scandinavian Journal of Medicine & Science in Sports.* 2013;23(1):57-65.
39. Bazanova OM, Vernon D. Interpreting EEG alpha activity. *Neuroscience & Biobehavioral Reviews.* 2014;44:94-110.

Chapter 6: General discussion

Main research findings

This PhD thesis's overall purpose was to contribute to clinical decision-making and functional performance testing across the sports injury spectrum. Specifically, the three major objectives of this thesis involved:

(1) establishing scientifically sound criteria to substantiate return-to-sport decisions following lateral ankle sprains,
(2) mapping the reliability characteristics of a new neurocognitive functional performance test: the reactive balance test,
(3) exploring electrophysiological brain changes induced by various fatigue types when participants performed the Y-balance test and reactive balance test.

Chapter 2 showed that no scientifically sound and prospectively determined return-to-sport criteria following lateral ankle sprain injury exist. This was because not one original research study prospectively applied a criteria-based return-to-sport decision-making process for lateral ankle sprain injury patients [1]. Nevertheless, 47 questionnaires and a combined total of 45 clinical and functional performance tests were identified during the systematic search process. These questionnaires and tests could be relevant during the rehabilitation process and potentially inform return-to-sport decisions following a lateral ankle sprain. Following the most recent scientific literature and insights combined with the extracted questionnaires and tests, I provided rationales and considerations for return-to-sport decision-making following lateral ankle sprain injury while also suggesting potential return-to-sport variables for future research.

The reliability study presented in **Chapter 3** is the first one to assess test-retest, intra- and inter-rater reliability of the reactive balance test within a generic recreationally trained population [2]. The results showed excellent intra- and inter-rater reliability for both outcomes (i.e. visuomotor response time and accuracy). However, test-retest reliability showed good reliability for visuomotor response time and moderate reliability for accuracy.

To explore the electrophysiological brain changes induced by various fatigue type, we performed two randomized cross-over trials. The third study in this thesis **(Chapter 4)** was designed to evaluate the impact of mental fatigue on electrophysiological brain measurements during Y-balance test and reactive balance test performance [3]. Even though mental fatigue was successfully induced, it did not affect Y-balance test performance. However, an increase in prefrontal cortex theta activity was observed when performing the Y-balance test in a mentally fatigued state. Which means mental fatigue was successfully induced and might suggest a lower availability of attentional resources and poorer decision-making. Regarding reactive balance test performance, the accuracy was compromised due to mental fatigue. No changes in visuomotor reaction time and electrophysiological brain outcome measures were found following the mental fatigue intervention. This infers that negative alterations at the psychological and physiological level due to a prolonged cognitive task may not be detrimental for Y-balance test performance. Yet, mental fatigue induced changes tend to appear when adding a neurocognitive task to this traditional functional performance test.

In **Chapter 5**, similar findings occurred in Y-balance test performance and reactive balance test performance when exposing the participants to acute physical fatigue. The results of current study showed acute physical fatigue to impair accuracy of the reactive balance test while Y-balance test performance and visuomotor response time of the reactive balance test did not significantly change [4]. Nevertheless, the underlying changes at the peripheral and central physiological level completely differed from the previous mental fatigue study. During the execution of both tests, acute physical fatigue induced alterations in electrophysiological brain outcome measures in line with previous Wingate literature. Higher α power in the prefrontal cortex, motor cortex and posterior parietal cortex, and higher β power in the prefrontal and posterior parietal cortex were observed during the execution of the Y-balance test in a fatigued state. Following acute physical fatigue, α and β power increments were found in the posterior parietal cortex and the prefrontal cortex during the reactive balance test execution, respectively. These cortical activity changes might partially correlate to the decrement in reactive balance test performance following acute physical fatigue. Regardless of the vast amount of physiological changes at the peripheral and central level, no alterations in Y-balance performance were witnessed.

In the following section, I will put the individual studies' results in context and discuss their contribution to clinical practice and research.

Criteria-based return-to-sport decision-making following lateral ankle sprain injury

Lateral ankle sprain injuries have the highest recurrence rate of all musculoskeletal sports injuries, mainly due to the residual sensorimotor impairments at the time of the return-to-sport decision [5-17]. Throughout the systematic review's search process, I acquired plenty of valuable information (i.e. 47 questionnaires, 45 tests). However, no prospectively determined return-to-sport criteria following lateral ankle sprain injury are available at the moment (**Chapter 2**) [1].

A remarkable finding was the abundant use of the outcome measure “time to return-to-sport, work or play” following a lateral ankle sprain injury in contrast to no articles studying an objective return-to-sport decision-making approach [18-30]. This is probably because lateral ankle sprain injuries are generally assumed to be minor injuries, even though the evidence contradicts this line of thought [5-11,13,31-46]. Individuals who sustained a lateral ankle sprain injury need adjusted care to resolve impairments before they would be allowed to return-to-sport. Successful return-to-sport should, therefore, not be measured by how fast an individual can return. The following three parameters should at least be incorporated when defining successful return-to-sport:

(1) whether the individual retains (minimal to) no residual impairments at the time of the decision,
(2) the individual can remain injury-free,
(3) the individual can achieve performance levels equal to or greater than before the injury.

Although time and time pressure will always be an inherent characteristic of the rehabilitation process and return-to-sport continuum, it should never be the primary outcome variable when making a return-to-sport decision. Therefore, the authorship team and I decided to advise against the inclusion of the outcome "time to return-to-sport" when making a return-to-sport decision.

Seven different categories were put together and contained variables to consider in the context of return sport decision-making after a lateral ankle sprain injury. The seven categories encompass "Predisposing factors increasing the (re)injury risk and prognostic factors increasing the risk of developing CAI", "Ligament healing, ankle laxity and arthrokinematics", "Clinical tests and patient-reported outcomes", "Functional and sport-specific performance tests", "Load monitoring", "Psychological and psychosocial factors", and "Decision modifying variables". These categories were based on the multitude of questionnaires and tests identified during the systematic search process in conjunction with relevant scientific literature. Special attention was paid to align these categories with the biopsychosocial framework, the 2016 return-to-sports consensus statement and the new insights on complexity within the sports injury domain, which means that one outcome can never contain all the important information to make a well-informed return-to-sport decision. Therefore, it is advised to select multiple outcomes measures covering the patient's most relevant biological, psychological, and social aspects when making this decision.

This information can already support clinicians in making more objective and better-informed return-to-sport decisions following lateral ankle sprain injury, even when no scientifically proven criteria are available at the moment. Furthermore, the systematic review [1] can help researchers set up prospective research designs to test the relevance and practical feasibility of criteria-based return-to-sport decisions following lateral ankle sprain injuries. It gives them a wide overview of which potential variables and outcome measures could be included when making choices in the design of the return-to-sport decision.

Functional performance tests integrating reactive & decision-making aspects of the sport context

New functional performance tests more closely approximating the sport context are demanded [47-50]. We recently developed and validated a functional performance test that included reactive & decision-making elements, namely, the reactive balance test [51]. Nevertheless, implementing the reactive balance test in scientific research or clinical practice would only be justified when its basic clinimetric properties are researched and show at least an acceptable quality level. The reliability study (**Chapter 3**) in a generic recreationally trained population indicated to let the same rater evaluate the outcome measures of the reactive balance test. This is because the excellent ICC values and the 95% confidence intervals show marginally better intra-rater reliability results than inter-rater reliability. Given that the test-retest reliability ranged from moderate to good over a clinically relevant period indicates that the test is currently not appropriate for individual analyses or decisions over time within a generic recreationally trained population. Yet, it makes the reactive balance test suited for scientific research performing analyses over time at the group level [2].

These are only the first steps in the development and description of the reactive balance test. Before making recommendations for its use in clinical practice, it will be important to examine this test further. For example, the reliability in more specific populations should be assessed. Small adjustments can be made to the test protocol to increase operational convenience. Furthermore, the reactive balance test and other neurocognitive functional performance tests [52] could be incorporated in prospective clinical studies to determine whether they provide added value in injury risk assessments, follow-up of rehabilitation progress, or the return-to-sport decision-making process. Especially since poorer neurocognitive performance and the addition of cognitive tasks to physical performance have already been linked to an increased sports injury risk [53-57].

Developing functional performance tests with reactive elements and decision-making steps associated with real sport situations is a relatively new field. The ability to create such tests has been made possible due to technological advancements that made it feasible to easily train adaptability and neurocognitive components in clinical practice (e.g. Fitlight Trainer™, Blazepod™). This type of equipment can thus also be used to develop new functional performance tests. Yet, the adaptability and neurocognition constructs reach further than adding simple visuomotor tasks to already existing functional performance tests. Therefore, more cost-effective and alternative solutions (e.g. simple virtual reality solutions, sport-specific test development) are other interesting routes to explore in the meantime.

To the best of the author's knowledge, the reactive balance test [2,51] and four neurocognitive hop tests [52] are currently the only existing functional performance tests addressing the demand of the 2016 return-to-sports consensus statement to bring functional performance tests closer to the sports context [50]. Together, these neurocognitive functional performance tests might be used in a complementary way in scientific research since the neurocognitive hop tasks can be classified as discrete neurocognitive tasks. In contrast, the reactive balance test covers the continuous nature of the task spectrum. These tests provide innovative methods to support researchers when investigating an individual's injury risk, rehabilitation progress, or return-to-sport ability.

Translational research: bridging the gap between fundamental research & clinical practice

Fundamental research studies are conducted in a well-controlled (laboratory) environment with technical outcome measures (e.g. centre of pressure changes, limits of stability). This means that their results are not directly transferable to clinical practice and regularly contradict the clinical practice observations. This predicament is commonly referred to as 'the gap' between fundamental research and clinical practice. Within the functional performance test domain, clinicians are constantly confronted with this situation. Therefore, a clear need exists for translational research examining fundamental issues that can be translated and adapted to clinical practice. The following section highlights how the studies described in **Chapters 4 & 5** contributed to this objective by exploring electrophysiological brain changes induced by various fatigue types when participants performed the Y-balance test and reactive balance test.

Previous studies observed conflicting results when researching fatigue's impact on reach distances of the SEBT and YBT [58-63]. Even though these studies always induced fatigue through physical exertion, both the mental fatigue and acute physical fatigue study did not find a deterioration of reach distances in YBT performance. In this way, these two studies further contribute to this conflicting body of literature. In contrast to my studies, most studies do not include any outcome measures to assess the underlying physiological processes. One can only state that applying different fatigue protocols and including different populations generates these differences in results. This limits our understanding and interpretation of which underlying fatigue mechanisms are responsible for the decline or preservation in SEBT and YBT performance.

At the brain level during YBT performance, the observed θ power increment in the prefrontal cortex when mentally fatigued and both the α and β power increments in the regions of interest after a physically fatiguing task are in line with previous mental fatigue [64-68] and acute physical fatigue [69-71] research, respectively. This is a positive key finding of my studies. This allows us to interpret the previously reported results and general insights in electrophysiological brain functioning when discussing the specific changes in fatigued individuals performing the YBT. The changes in θ power at the prefrontal cortex caused by mental fatigue are associated with attentional deficits, impaired decision-making, and a reduced arousal level [64,67,72,73]. In contrast, the alterations in α and β power across the whole brain due to an acute physically fatiguing task are hypothesised to display increased cognitive processing [69-71]. Nevertheless, these fatigue induced spectral power increments might encompass a myriad of physiological and psychological changes [70]. Therefore, one should always cautiously interpret the results and advocate for complementary research to verify, question or reject these assumptions and interpretations. Regardless of these central changes, YBT performance was not affected. A potential explanation might be that the YBT requires little attentional resources, cognitive processing and decision-making, given that it is performed in a predetermined order with all movements being pre-planned. Furthermore, the YBT also does not contain reactive elements and instant decision-making aspects in contrast to the RBT, making it potentially more likely for the individual to maintain YBT performance. It might be good for clinicians to know and reassure them that the YBT is quite a robust functional performance test and is not easily affected by fatigue-induced impairments at the physiological and psychological level. Therefore, the YBT might be a good functional performance test to monitor individuals over time, whilst it might be a suboptimal functional performance test to assess acute fatigue-related impairments.

The RBT is the first neurocognitive functional performance test exposed to different types of fatigue whilst also measuring the brain's electrophysiological activity. Following both fatigue interventions, RBT accuracy decreased consistently with a maintenance of RBT visuomotor reaction time. These results are partially in line with previous research examining the impact of fatigue on neurocognitive outcomes. In most studies, a deterioration of accuracy coincides with a worsening in visuomotor response time, but occasionally only one neurocognitive outcome measure is affected by the fatigue intervention [64-68,74-77]. Even though both studies found similar RBT performance results, the underlying mechanisms leading to these changes are probably different. Mental fatigue is known to induce θ and α spectral power increments at the cortical level. These alterations are linked with lower availability of attentional resources and impaired decision-making [64-68]. However, I did not observe an increment of θ or α spectral power during RBT performance due to mental fatigue. Nevertheless, several psychological changes were registered in the participant group following the mental fatigue intervention (e.g. increased M-VAS en NASA-TLX). It is unlikely that the decrease in RBT accuracy can solely be attributed to psychological changes. Given the importance of signal processing in both neurocognitive and mental fatigue research, future research should further attempt to map potential mental fatigue induced brain changes that could be linked with changes in RBT accuracy. In the acute physical fatigue study, however, electrophysiological changes during RBT performance were detected. The observed changes were in line with previous Wingate literature and are associated with increased cognitive processing [69-71]. This implies that the combination of both peripheral and central acute physical fatigue-induced changes could have led to participants obtaining a lower accuracy during RBT performance. The RBT is thus able to detect subtle and less-subtle acute fatigue alterations at the behavioural level. Researchers and clinicians should be aware that the reliability over time of the RBT test only allows for analyses at the group level. The RBT might be suitable to detect acute (fatigue) alterations and impairments in contrast to the more traditional YBT. These results contribute to the foundation for future research to study the entire sports injury domain in innovative ways. Yet, it remains to be seen whether future research can obtain similar results in other neurocognitive functional performance tests or whether other independent research groups can reproduce these studies' results. Nonetheless, clinicians and researchers should be vigilant and carefully monitor each individual's status before executing the RBT, given that the RBT accuracy component is easily affected by underlying physiological and psychological changes.

In summary, mental fatigue does not impact YBT performance, even when underlying physiological and psychological changes are present. To make a statement on acute physical fatigue, too much conflicting results are available at the moment regarding YBT performance. Clinicians and researchers should not be concerned about YBT performance being affected when individuals are mentally fatigued. In case of looming physical fatigue, clinicians should be more prudent when the goal is to let individuals perform the YBT in a non-fatigued state. Nevertheless, the RBT can detect acute and subtle (fatigue) changes at the group level resulting in a decrease in accuracy. These are only the first small steps into the translational research domain encompassing functional performance tests. In the end, translational research might grant researchers and clinicians an improved understanding of fundamental aspects in daily practice and ultimately lead to the development of better tools within the sports injury domain.

Strengths and limitations

This PhD thesis's main research findings can support clinicians and researchers in clinical decision-making and functional performance testing across the sports injury spectrum. They also provide a solid foundation for future clinically relevant research. Valuable progress was made considering:

(1) the call for objective return-to-sport decision-making criteria following common sports injuries,
(2) the need for functional performance tests integrating neurocognition and adaptability,
(3) the lack of translational research and application of contextual factors during functional performance testing.

The main limitation of the current scientific literature (**Chapter 2**) is that there are no studies concerning objective and scientifically sound return-to-sport criteria following lateral ankle sprain injuries. Also, the outcome "time to return-to-sport, work or participation" was abundantly present in the screened literature. The main limitation of the systematic literature review is that the proposed categories of return-to-sport variables are merely derived from relevant scientific research encompassing questionnaires and tests utilised during the rehabilitation of individuals who incurred a lateral ankle sprain injury [1]. Nevertheless, this chapter provides clinicians with a clear overview of potential tools to support current rehabilitation progress monitoring and return-to-sport decision-making whilst also providing researchers with a strong foundation for future research on return-to-sport criteria following lateral ankle sprains. Several minor limitations worth considering are (1) the use of the terminology "lateral ankle sprain injury" [78,79], (2) implementational issues [80-83], and (3) perverse incentives [82-84].

Two population-based limitations in my research studies (**Chapter 3, 4 and 5**) encompass the inclusion of recreational athletes and the selection of a relatively small sample size for each study. Including recreational athletes (= a potential heterogeneous group in athletic ability and fitness level) may have consequences for interpreting the results. For instance, ICC estimations are specific to the used population, and the fatigue interventions can have a different impact on less trained and very well-trained recreational athletes. The main rationales to include recreational athletes were transferability and representativeness since they comprise the largest group within the practice of organised sport. Also, participants had to fill in a simplified version of the International Physical Activity Questionnaires during the familiarisation trials. This was for us to get insight into their physical activity and fitness level. Albeit the large variability in practised sports, the results of this questionnaire showed that the included participants had quite similar physical activity and fitness levels with only a few outliers. The main concerns regarding the relatively small sample sizes are the increased probability of a false positive significant effect and the lower probability of observing a true effect [85]. To mitigate the probability of these statistical threats, I always conducted sample size calculations before the required documents for study approval were submitted to the medical ethics committee. Furthermore, I also included additional participants on top of the minimum number of required participants to consolidate the statistical analyses further. An additional reason was to avoid possible detrimental consequences for the results' statistical interpretation due to participants potentially dropping out of the experiments. Given that all of my research studies include more participants than the minimum required number of participants calculated by the sample size calculations, I can state with a reasonable degree of certainty that the aforementioned statistical risks have been kept to a minimum.

Another possible limitation could be that my interpretation of "translational research" in the conducted fatigue studies (**Chapter 4 & 5**) was too laboratory oriented. Nevertheless, I assume that translational research involves a broad spectrum ranging from 'field and clinical studies including fundamental research outcome measures to better comprehend the observed findings in clinical practice' to 'laboratory-based studies researching fundamental issues combined with clinical practice-based outcome measures'. These fatigue studies are thus more in line with the latter context. The main rationales to perform these studies within this context were: standardisation and feasibility. The standardisation rationale mostly applies to fatigue interventions. First and foremost, laboratory settings are more appropriate to induce fatigue in a standardised and controlled manner. The major disadvantage of field studies that induce fatigue through real-life situations is the heterogeneity in the fatigue intervention parameters, the amount of fatigue induced, and the effect of fatigue on the outcome measures of interest. The feasibility rationale is most applicable to the used EEG device and measurements. Despite the availability of mobile/wireless EEG devices on the market, I had a more traditional EEG device at my disposal without these wireless functions. The use of a more traditional EEG device makes it impractical to carry out field studies. These considerations contributed to my decision to conduct fatigue studies in a laboratory setting rather than choosing a more field study design.

Practical implications

- *Time to retire "time to return-to-sport" as a surrogate measure for a successful return-to-sport* – Successful return-to-sport should not be measured by how fast an individual can return, but whether the individual retains (minimal to) no residual impairments, can remain injury-free and achieve performance levels equal or greater than before the injury.
- *Never risk your reputation on one outcome* – Since humans can be regarded as complex adaptative systems, it would be unwise to base injury risk profiles, rehabilitation monitoring strategies, and return-to-sport decisions on only one outcome. One outcome can impossibly contain all the important information to make a well-informed risk profile or decision. Therefore, it is best to select multiple outcomes measures covering biological, psychological and social characteristics.
- *To measure is to know* – Even though no scientific return-to-sport criteria for individuals who suffered a lateral ankle sprain injury exist, practitioners should use both objective and subjective tools to support their return-to-sport decision. I provided an assortment of tools (**Chapter 2**) to assist practitioners in their return-to-sport decision-making process following lateral ankle sprain injury and possibly for chronic ankle instability populations.
- *The long and winding road* – Although neurocognitive functional performance tests are relatively new and their value for clinical practice still has to be demonstrated through high-quality research, these newly developed tests and variations of these tests can already be used as additional exercises in clinical

practice in the context of improving adaptability and neurocognitive functions. The road from development to implementation of new tests takes time. The same can be implied for developing and implementing scientifically sound return-to-sport criteria following common sports injuries.

- *Innovation is a process that happens both top-down and bottom-up* – I hope to inspire practitioners to develop their own neurocognitive functional performance tests or other adaptability tests and to collaborate with researchers. This way, we create a healthy relationship and exchange between clinical practice and research. Of course, these tests' clinimetric properties should be carefully mapped before implementing them in research and clinical practice. Nevertheless, practitioners might be better positioned to create new functional performance tests since they know what is currently missing in clinical practice to improve patient care and decision-making.
- *There is more to it than meets the eye* – Concerning the Y-balance test, the fatigue studies showed that changes at the underlying central and peripheral level do not always result in alterations at the behavioural/performance level. However, the reactive balance test was susceptible for both fatigue interventions, resulting in a deterioration of accuracy, while underlying mechanisms were substantially different. In summary, it is not because nothing changes at the higher system level (i.e. Y-balance test performance) that nothing changes at the system's lower levels. On the other hand, different changes at the lower system level can produce similar results at the system's higher-level (i.e. reactive balance performance).
- *Reproducibility of results* – The cortical changes during Y-balance test and reactive balance test performance due to the fatigue interventions were in line with previous scientific research, which enables practitioners to carefully extrapolate earlier fundamental research findings to the functional performance test domain.

Future perspectives and outlook

"The deeper the foundations, the stronger the fortress." – This thesis has contributed to the foundations for future fundamental, translational and clinical research. It also uncovered some areas within the foundations of the sports injury domain that require improvement. The first area future research could easily improve, is the mapping of clinimetric properties of functional performance tests in general and specific contexts because there is a clear lack of available scientific information on these properties [47,48]. This hinders both researchers and clinicians in selecting appropriate functional performance tests as well as interpret them correctly.

Another area for future research is developing objective return-to-sport criteria following common sports injuries to offer clinicians a solid basis to make return-to-sport decisions and let athletes return-to-sport more safely. Currently, research on return-to-sport decision-making after incurring anterior cruciate ligament injuries [86-92] and hamstring strain injuries [93-98] receives the most attention in this domain. In contrast, most of the other sports injuries remain untouched. Furthermore, several concerns and barriers (e.g. no reduction in injury recurrence rate, not practically feasible, unfavourable cost-benefit analysis) could halt the development and implementation of a criteria-based return-to-sport decision-making approach. Concerning return-to-sport decision-making following lateral ankle sprains, a worldwide research enterprise has been undertaken by the International Ankle Consortium. The International Ankle Consortium started an international Delphi study to develop a worldwide consensus of opinion on possible relevant variables and outcome measures in the context of deciding whether an individual is ready to return-to-sport following a lateral ankle sprain injury [99]. The questionnaire used in this international Delphi study was developed based on the systematic review included in this thesis [1]. The preliminary findings of this Delphi study prioritise the need to assess the performance of sport-specific/athletic skills, pain, local muscle function, ankle range of motion, balance and proprioception, and psychological readiness when making a return-to-sport decision. Together, the systematic review [1] and the aforementioned Delphi study [99] provide researchers with an overview of possible suitable variables for return-to-sport criteria. This should help facilitate future prospective cohort studies within this domain. Besides focusing on anterior cruciate ligament injuries, hamstring strain injuries, and lateral ankle sprain injuries, future research should also focus on other common and less common sports injuries to benefit all stakeholders involved in the return-to-sport process.

Simultaneously, the sports injury domain shifted its focus towards the exploration and utilisation of more advanced research designs [100,101] and analyses [102,103]. Despite this positive evolution, it is necessary to acknowledge that fundamental and translational research are still very much needed and still play an important role in the sports injury domain. All the aforementioned potential avenues for future research would further contribute to reinforcing the foundations of the sports injury domain. These are essential for future field studies or future studies including more advanced research designs and analyses.

"No one can whistle a symphony. It takes a whole orchestra to play it." – A high need exists for more collaboration within the sports injury domain. An interesting observation is that practitioners are seldomly invited to be involved in the development of research, even though their clinical experience and expertise are most suited to support the field's needs. Their input could be most valuable when making decisions on the research design to be in line with daily clinical practice as much as possible or to help uncover questions clinicians would like to have answers to.

Furthermore, a collaboration between research groups studying similar topics and working together with experts in other domains (e.g. statisticians, neuroscientists, engineers) are two aspects that could be improved. Whether it would be fundamental research or practical research, the inclusion of experts outside the sports injury domain could result in more meaningful research studies and questions with better research designs. This could further lead to upgraded analyses techniques and more accurate interpretations of the study results. The collaboration between research groups studying similar topics could have potential benefits for progress in research quality and clinical practice. This could be achieved by sharing knowledge and insights, but more so by undertaking multicentre studies together, resulting in larger sample sizes and rendering more meaningful results for clinical practice. In summary, research groups and institutes should make greater efforts to include practitioners in research, consult experts outside their domain, and set up collaborative initiatives with compatible research groups; Come Together, Right Now!

"The only thing that is constant is change." – Within the context of this thesis, technological advances (e.g. wearable sensors, wireless monitoring systems) will further transform the sports injury domain from research to clinical practice. Research on the development, value and implementation of neurocognitive functional performance tests is only in its infancy. Yet, these newly developed tests could offer innovative ways to assess patients and participants within injury prevention, rehabilitation and return-to-sport decision-making contexts. Therefore, prospective studies should research whether neurocognitive functional performance tests could be of value when screening for sports injury risk, assessing residual impairments post-injury, monitoring rehabilitation progress, and supporting the return-to-sport decision-making process. An additional research avenue might be to apply relevant contextual factors (e.g. fatigue) to functional performance testing throughout the sports injury continuum with the rationale to bring functional performance testing closer to the individual's relevant sport context. And by doing so, exposing quantitative or qualitative deficits that might alter injury risk, rehabilitation and return-to-sport decisions. Of course, a colossal challenge will be to translate such a tailored approach to clinical practice and develop clinician-friendly tools for practitioners to facilitate implementation and interpretation of the acquired results. Furthermore, the brain is gradually claiming the centre of attention in ligament injury research caused by sports participation. Hypotheses and preliminary (central) neuroplasticity results after ligament injury have been discussed [104,105]. These novel insights open up perspectives for fundamental, translational and practical research, and change how we screen, test, rehabilitate and train these individuals. Daunting but fascinating times lie ahead!

General Conclusion

This PhD thesis's overall purpose was to contribute to clinical decision-making and functional performance testing across the sports injury spectrum. The three primary objectives of this thesis involved:

(1) establishing scientifically sound criteria to substantiate return to sport decisions following lateral ankle sprains,
(2) mapping the reliability characteristics of a new neurocognitive functional performance test: the reactive balance test,
(3) exploring electrophysiological brain changes induced by various fatigue types when participants performed the Y-balance test and reactive balance test.

An overview of the research findings of this dissertation show that no scientifically sound return to sport criteria following lateral ankle sprain injury are currently available (**Chapter 2**). Therefore, we provided an overview of the relevant retrieved questionnaires, clinical assessment measures, functional and sport-specific performance tests within ankle sprain populations. This chapter also encompasses rationales and considerations for return to sport decision-making following lateral ankle sprain injury.

The reactive balance test has acceptable to excellent reliability characteristics and, therefore, is suited for performing analyses over time at the group level (**Chapter 3**). Since the values show marginally better results for intra-rater reliability than inter-rater reliability, preferably the same rater should evaluate the outcome measures of the reactive balance test. **Chapter 4 & 5** illustrate that mental and acute physical fatigue do not impact YBT performance, even when underlying peripheral and central (electro)physiological, and psychological changes are present. Only an increase in prefrontal cortex theta activity was observed when performing the Y-balance test in a mentally fatigued state. In contrast, higher α power in the prefrontal cortex, motor cortex and posterior parietal cortex and higher β power in the prefrontal and posterior parietal cortex were observed during the Y-balance execution test in an acute physical fatigued state. The reactive balance test can detect fatigue changes at the group level culminating in a decrease in accuracy. When mentally fatigued, no significant changes at the electrophysiological brain level were measured. Following acute physical fatigue, α and β power increments were found in the posterior parietal cortex and the prefrontal cortex during the reactive balance test execution, respectively.

This thesis contributed to the foundations for future fundamental, translational and clinical research. It also uncovered areas within the foundations of the sports injury domain that require improvement.

References

1. Tassignon B, Verschueren J, Delahunt E, Smith M, Vicenzino B, Verhagen E, et al. Criteria-based return to sport decision-making following lateral ankle sprain injury: a systematic review and narrative synthesis. Sports Med. 2019 Feb 11;49(4):601-19.

2. Tassignon B, Verschueren J, De Wachter J, Maricot A, De Pauw K, Verhagen E, et al. Test-retest, intra- and inter-rater reliability of the reactive balance test in healthy recreational athletes. Physical therapy in sport : official journal of the Association of Chartered Physiotherapists in Sports Medicine. 2020 Aug 23;46:47-53.

3. Tassignon B, Verschueren J, De Pauw K, Roelands B, Van Cutsem J, Verhagen E, et al. Mental fatigue impairs clinician-friendly balance test performance and brain activity. Translational Sports Medicine. 2020;3(6):616-25.

4. Tassignon B, Verschueren J, De Pauw K, Verhagen E, Meeusen R. Acute fatigue alters brain activity and impairs reactive balance test performance. Translational Sports Medicine. 2021;n/a(n/a).

5. Beynnon BD, Murphy DF, Alosa DM. Predictive factors for lateral ankle sprains: A literature review. Journal of Athletic Training. 2002 Oct-Dec;37(4):376-80.

6. Bahr R, Bahr IA. Incidence of acute volleyball injuries: A prospective cohort study of injury mechanisms and risk factors. Scandinavian Journal of Medicine & Science in Sports. 1997 Jun;7(3):166-71.

7. Gribble PA, Bleakley CM, Caulfield BM, Docherty CL, Fourchet F, Fong DTP, et al. Evidence review for the 2016 International Ankle Consortium consensus statement on the prevalence, impact and long-term consequences of lateral ankle sprains. British Journal of Sports Medicine. 2016 Dec;50(24):1496-+.

8. Swenson DM, Yard EE, Fields SK, Comstock RD. Patterns of Recurrent Injuries Among US High School Athletes, 2005-2008. American Journal of Sports Medicine. 2009 Aug;37(8):1586-93.

9. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: Summary and recommendations for injury prevention initiatives. Journal of Athletic Training. 2007 Apr-Jun;42(2):311-9.

10. Malliaropoulos N, Ntessalen M, Papacostas E, Longo UG, Maffulli N. Reinjury After Acute Lateral Ankle Sprains in Elite Track and Field Athletes. American Journal of Sports Medicine. 2009 Sep;37(9):1755-61.

11. Konradsen L, Bech L, Ehrenbjerg M, Nickelsen T. Seven years follow-up after ankle inversion trauma. Scandinavian Journal of Medicine & Science in Sports. 2002 Jun;12(3):129-35.

12. Steib S, Zech A, Hentschke C, Pfeifer K. Fatigue-Induced Alterations of Static and Dynamic Postural Control in Athletes With a History of Ankle Sprain. Journal of Athletic Training. 2013 Mar-Apr;48(2):203-8.

13. McKay GD, Goldie PA, Payne WR, Oakes BW. Ankle injuries in basketball: injury rate and risk factors. British Journal of Sports Medicine. 2001 Apr;35(2):103-8.

14. Boyce SH, Quigley MA, Campbell S. Management of ankle sprains: a randomised controlled trial of the treatment of inversion injuries using an elastic support bandage or an Aircast ankle brace. British Journal of Sports Medicine. 2005 Feb;39(2):91-6.

15. McKay G, Goldie P, Payne WR, Oakes BW, Watson LF. A prospective study of injuries in basketball: A total profile and comparison by gender and standard of competition. Journal of Science and Medicine in Sport. 2001 Jun;4(2):196-211.

16. van der Wees PJ, Hendriks EJM, Jansen MJ, van Beers H, de Bie RA, Dekker J. Adherence to physiotherapy clinical guideline acute ankle injury and determinants of adherence: a cohort study. Bmc Musculoskeletal Disorders. 2007 May;8:7.

17. McCann R, Kosik K, Terada M, Gribble P. Residual Impairments and Activity Limitations at Return to Play from a Lateral Ankle Sprain. International Journal of Athletic Therapy & Training. 2018 Mar;23(2):83-8.

18. Baumbach SF, Fasser M, Polzer H, Sieb M, Regauer M, Mutschler W, et al. Study protocol: the effect of whole body vibration on acute unilateral unstable lateral ankle sprain- a biphasic randomized controlled trial. BMC Musculoskelet Disord. 2013 Jan 14;14:22.

19. Bendahou M, Khiami F, Saidi K, Blanchard C, Scepi M, Riou B, et al. Compression stockings in ankle sprain: a multicenter randomized study. Am J Emerg Med. 2014 Sep;32(9):1005-10.

20. Beynnon BD, Renstrom PA, Haugh L, Uh BS, Barker H. A prospective, randomized clinical investigation of the treatment of first-time ankle sprains. Am J Sports Med. 2006 Sep;34(9):1401-12.

21. Gunay S, Karaduman A, Ozturk BB. Effects of Aircast brace and elastic bandage on physical performance of athletes after ankle injuries. Acta Orthop Traumatol Turc. 2014;48(1):10-6.

22. Hubbard TJ, Hicks-Little CA. Ankle ligament healing after an acute ankle sprain: an evidence-based approach. J Athl Train. 2008 Sep-Oct;43(5):523-9.

23. Hunt KJ, Hurwit D, Robell K, Gatewood C, Botser IB, Matheson G. Incidence and Epidemiology of Foot and Ankle Injuries in Elite Collegiate Athletes. Am J Sports Med. 2017 Feb;45(2):426-33.

24. Kerkhoffs GM, Rowe BH, Assendelft WJ, Kelly KD, Struijs PA, van Dijk CN. Immobilisation for acute ankle sprain. A systematic review. Arch Orthop Trauma Surg. 2001 Sep;121(8):462-71.

25. Kerkhoffs GM, Struijs PA, Marti RK, Assendelft WJ, Blankevoort L, van Dijk CN. Different functional treatment strategies for acute lateral ankle ligament injuries in adults. Cochrane Database Syst Rev. 2002(3):Cd002938.

26. Kerkhoffs GM, Rowe BH, Assendelft WJ, Kelly K, Struijs PA, van Dijk CN. Immobilisation and functional treatment for acute lateral ankle ligament injuries in adults. Cochrane Database Syst Rev. 2002(3):Cd003762.

27. Kerkhoffs GM, Handoll HH, de Bie R, Rowe BH, Struijs PA. Surgical versus conservative treatment for acute injuries of the lateral ligament complex of the ankle in adults. Cochrane Database Syst Rev. 2007 Apr 18(2):Cd000380.

28. Mendel FC, Dolan MG, Fish DR, Marzo J, Wilding GE. Effect of high-voltage pulsed current on recovery after grades I and II lateral ankle sprains. J Sport Rehabil. 2010 Nov;19(4):399-410.

29. Petrella RJ, Petrella MJ, Cogliano A. Periarticular hyaluronic acid in acute ankle sprain. Clin J Sport Med. 2007 Jul;17(4):251-7.

30. Wilson RW, Gansneder BM. Measures of functional limitation as predictors of disablement in athletes with acute ankle sprains. J Orthop Sports Phys Ther. 2000 Sep;30(9):528-35.

31. Doherty C, Delahunt E, Caulfield B, Hertel J, Ryan J, Bleakley C. The Incidence and Prevalence of Ankle Sprain Injury: A Systematic Review and Meta-Analysis of Prospective Epidemiological Studies. Sports Medicine. 2014 Jan;44(1):123-40.

32. Drakos MC, Domb B, Starkey C, Callahan L, Allen AA. Injury in the national basketball association: a 17-year overview. Sports Health. 2010 Jul;2(4):284-90.

33. Fong DTP, Hong YL, Chan LK, Yung PSH, Chan KM. A systematic review on ankle injury and ankle sprain in sports. Sports Medicine. 2007;37(1):73-94.

34. Jacobs CL, Hincapie CA, Cassidy JD. Musculoskeletal injuries and pain in dancers: a systematic review update. J Dance Med Sci. 2012;16(2):74-84.

35. Waterman BR, Owens BD, Davey S, Zacchilli MA, Belmont PJ. The Epidemiology of Ankle Sprains in the United States. Journal of Bone and Joint Surgery-American Volume. 2010 Oct;92A(13):2279-84.

36. Wolfenden HEG, Angioi M. Musculoskeletal Injury Profile of Circus Artists A Systematic Review of the Literature. Medical Problems of Performing Artists. 2017 Mar;32(1):51-9.

37. Cumps E, Verhagen E, Meeusen R. Prospective epidemiological study of basketball injuries during one competitive season: Ankle sprains and overuse knee injuries. Journal of Sports Science and Medicine. 2007 Jun;6(2):204-11.

38. Delahunt E, Coughlan GF, Caulfield B, Nightingale EJ, Lin CWC, Hiller CE. Inclusion Criteria When Investigating Insufficiencies in Chronic Ankle Instability. Medicine and Science in Sports and Exercise. 2010 Nov;42(11):2106-21.

39. Hertel J. Functional anatomy, pathomechanics, and pathophysiology of lateral ankle instability. Journal of Athletic Training. 2002 Oct-Dec;37(4):364-75.

40. Hiller CE, Kilbreath SL, Refshauge KM. Chronic Ankle Instability: Evolution of the Model. Journal of Athletic Training. 2011 Mar-Apr;46(2):133-41.

41. Harrington KD. Degenerative arthritis of the ankle secondary to long standing lateral ligament instability. J Bone Joint Surg. 1979;61A:354-61.

42. Landeros O, Frost HM, Higgins CC. Post traumatic anterior ankle instability. Clin Orthop. 1968;56:169-78.

43. Al-Mahrouqi MM, Macdonald DA, Vicenzino B, Smith MD. Physical Impairments in Adults With Ankle Osteoarthritis: A Systematic Review and Meta-analysis. Journal of Orthopaedic & Sports Physical Therapy. 2018 Jun;48(6):449-+.

44. Birrer RB, Fani-Salek MH, Totten VY, Herman LM, Politi V. Managing ankle injuries in the emergency department. Journal of Emergency Medicine. 1999 Jul-Aug;17(4):651-60.

45. Gribble PA, Bleakley CM, Caulfield BM, Docherty CL, Fourchet F, Fong DTP, et al. 2016 consensus statement of the International Ankle Consortium: prevalence, impact and long-term consequences of lateral ankle sprains. British Journal of Sports Medicine. 2016 Dec;50(24):1493-5.

46. Feger MA, Glaviano NR, Donovan L, Hart JM, Saliba SA, Park JS, et al. Current Trends in the Management of Lateral Ankle Sprain in the United States. Clinical Journal of Sport Medicine. 2017 Mar;27(2):145-52.

47. Hegedus EJ, McDonough S, Bleakley C, Cook CE, Baxter GD. Clinician-friendly lower extremity physical performance measures in athletes: a systematic review of measurement properties and correlation with injury, part 1. The tests for knee function including the hop tests. Br J Sports Med. 2015 May;49(10):642-8.

48. Hegedus EJ, McDonough SM, Bleakley C, Baxter D, Cook CE. Clinician-friendly lower extremity physical performance tests in athletes: a systematic review of measurement properties and correlation with injury. Part 2-the tests for the hip, thigh, foot and ankle including the star excursion balance test. Br J Sports Med. 2015 May;49(10):649-56.

49. Glasgow P, Bleakley CM, Phillips N. Being able to adapt to variable stimuli: the key driver in injury and illness prevention? Br J Sports Med. 2013 Jan;47(2):64-5.

50. Ardern CL, Glasgow P, Schneiders A, Witvrouw E, Clarsen B, Cools A, et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. Br J Sports Med. 2016 Jul;50(14):853-64.

51. Verschueren J, Tassignon B, Pluym B, Van Cutsem J, Verhagen E, Meeusen R. Bringing context to balance: development of a reactive balance test within the injury prevention and return to sport domain. Arch Physiother. 2019;9(6):eCollection 2019.

52. Millikan N, Grooms DR, Hoffman B, Simon JE. The development and reliability of four clinical neurocognitive single-leg hop tests: implications for return to activity decision making. J Sport Rehabil. 2018 Nov 14:1-26.

53. Wilkerson GB, Mokha M. Neurocognitive reaction time predicts lower extremity sprains and strains. IJATT. 2012 Nov;17(6):4-9.

54. Swanik CB, Covassin T, Stearne DJ, Schatz P. The relationship between neurocognitive function and noncontact anterior cruciate ligament injuries. American Journal of Sports Medicine. 2007 Jun;35(6):943-8.

55. Herman DC, Barth JT. Drop-Jump Landing Varies With Baseline Neurocognition: Implications for Anterior Cruciate Ligament Injury Risk and Prevention. American Journal of Sports Medicine. 2016 Sep;44(9):2347-53.

56. Brown TN, Palmieri-Smith RM, McLean SG. Sex and limb differences in hip and knee kinematics and kinetics during anticipated and unanticipated jump landings: implications for anterior cruciate ligament injury. Br J Sports Med. 2009 Dec;43(13):1049-56.

57. Seymore KD, Cameron SE, Kaplan JT, Ramsay JW, Brown TN. Dual-task and anticipation impact lower limb biomechanics during a single-leg cut with body borne load. J Biomech. 2017 Dec 8;65:131-7.

58. Baghbani F, Woodhouse LJ, Gaeini AA. Dynamic postural control in female athletes and nonathletes after a whole-body fatigue protocol. Journal of Strength and Conditioning Research. 2016 Jul;30(7):1942-7.

59. McMullen KL, Cosby NL, Hertel J, Ingersoll CD, Hart JM. Lower Extremity Neuromuscular Control Immediately After Fatiguing Hip-Abduction Exercise. Journal of Athletic Training. 2011 Nov-Dec;46(6):607-14.

60. Zech A, Steib S, Hentschke C, Eckhardt H, Pfeifer K. Effects of localized and general fatigue on static and dynamic postural control in male team handball athletes. J Strength Cond Res. 2012 Apr;26(4):1162-8.

61. Whyte E, Burke A, White E, Moran K. A high-intensity, intermittent exercise protocol and dynamic postural control in men and women. J Athl Train. 2015 Apr;50(4):392-9.

62. Johnston W, Dolan K, Reid N, Coughlan GF, Caulfield B. Investigating the effects of maximal anaerobic fatigue on dynamic postural control using the Y-Balance Test. Journal of science and medicine in sport. 2018 Jan;21(1):103-8.

63. Armstrong R, Brogden CM, Milner D, Norris D, Greig M. The Influence of Fatigue on Star Excursion Balance Test Performance in Dancers. Journal of Dance Medicine & Science. 2018 Sep;22(3):142-7.

64. Boksem MAS, Meijman TF, Lorist MM. Effects of mental fatigue on attention: an ERP study. Brain Res Cogn Brain Res. 2005;25(1):107-16.

65. Pires FO, Silva-Júnior FL, Brietzke C, Franco-Alvarenga PE, Pinheiro FA, de França NM, et al. Mental Fatigue Alters Cortical Activation and Psychological Responses, Impairing Performance in a Distance-Based Cycling Trial. Front Physiol. 2018;9:227-.

66. Van Cutsem J, De Pauw K, Buyse L, Marcora S, Meeusen R, Roelands B. Effects of Mental Fatigue on Endurance Performance in the Heat. Medicine and Science in Sports and Exercise. 2017 Aug;49(8):1677-87.

67. Wascher E, Rasch B, Sänger J, Hoffmann S, Schneider D, Rinkenauer G, et al. Frontal theta activity reflects distinct aspects of mental fatigue. Biological psychology. 2014;96:57-65.

68. Käthner I, Wriessnegger SC, Müller-Putz GR, Kübler A, Halder S. Effects of mental workload and fatigue on the P300, alpha and theta band power during operation of an ERP (P300) brain–computer interface. Biological Psychology. 2014 2014/10/01/;102:118-29.

69. Crabbe JB, Dishman RK. Brain electrocortical activity during and after exercise: A quantitative synthesis. Psychophysiology. 2004;41(4):563-74.

70. Moraes H, Ferreira C, Deslandes A, Cagy M, Pompeu F, Ribeiro P, et al. Beta and alpha electroencephalographic activity changes after acute exercise. Arquivos de Neuro-Psiquiatria. 2007;65:637-41.

71. Enders H, Cortese F, Maurer C, Baltich J, Protzner AB, Nigg BM. Changes in cortical activity measured with EEG during a high-intensity cycling exercise. J Neurophysiol. 2016 Jan 1;115(1):379-88.

72. Klimesch W. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res Brain Res Rev. 1999 Apr;29(2-3):169-95.

73. Tops M, Boksem MA. Absorbed in the task: Personality measures predict engagement during task performance as tracked by error negativity and asymmetrical frontal activity. Cogn Affect Behav Neurosci. 2010 Dec;10(4):441-53.

74. Whyte EF, Gibbons N, Kerr G, Moran KA. Effect of a High-Intensity, Intermittent-Exercise Protocol on Neurocognitive Function in Healthy Adults: Implications for Return-to-Play Management After Sport-Related Concussion. Journal of sport rehabilitation. 2015 Nov 1;24(4).

75. Pavelka R, Třebický V, Třebická Fialová J, Zdobinský A, Coufalová K, Havlíček J, et al. Acute fatigue affects reaction times and reaction consistency in Mixed Martial Arts fighters. PloS one. 2020;15(1):e0227675.

76. Sieck DC, Ely MR, Romero SA, Luttrell MJ, Abdala PM, Halliwill JR. Post-exercise syncope: Wingate syncope test and visual-cognitive function. Physiol Rep. 2016 Aug;4(16).

77. Van Cutsem J, De Pauw K, Vandervaeren C, Marcora S, Meeusen R, Roelands B. Mental fatigue impairs visuomotor response time in badminton players and controls. Psychology of Sport and Exercise. 2019 2019/11/01/;45:101579.

78. Delahunt E, Gribble PA. Structured clinical assessment: a brake to stop the ankle joint 'rolling'. Br J Sports Med. 2018 Jun 9.

79. van Dijk CN, Vuurberg G. There is no such thing as a simple ankle sprain: clinical commentary on the 2016 International Ankle Consortium position statement. Br J Sports Med. England; 2017. p. 485-6.

80. O'Brien J, Hägglund M, Bizzini M. Implementing injury prevention – the rocky road from rct to realworld injury reduction. ASPETAR Sports Medicine Journal. 2018;7(16):70-6.

81. Finch C. A new framework for research leading to sports injury prevention. Journal of science and medicine in sport. 2006 May;9(1-2):3-9; discussion 10.

82. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. American journal of public health. 1999 Sep;89(9):1322-7.

83. Verhagen E, Voogt N, Bruinsma A, Finch CF. A knowledge transfer scheme to bridge the gap between science and practice: an integration of existing research frameworks into a tool for practice. Br J Sports Med. 2014 Apr;48(8):698-701.

84. Strathern M. 'Improving ratings': audit in the British University system. European Review. 1997;5(3):305-21.

85. Button KS, Ioannidis JPA, Mokrysz C, Nosek BA, Flint J, Robinson ESJ, et al. Power failure: why small sample size undermines the reliability of neuroscience. Nature Reviews Neuroscience. 2013 2013/05/01;14(5):365-76.

86. Dingenen B, Gokeler A. Optimization of the Return-to-Sport Paradigm After Anterior Cruciate Ligament Reconstruction: A Critical Step Back to Move Forward. Sports Med. 2017 Aug;47(8):1487-500.

87. Rambaud AJM, Ardern CL, Thoreux P, Regnaux JP, Edouard P. Criteria for return to running after anterior cruciate ligament reconstruction: a scoping review. Br J Sports Med. 2018 May 2.

88. Gokeler A, Welling W, Zaffagnini S, Seil R, Padua D. Development of a test battery to enhance safe return to sports after anterior cruciate ligament reconstruction. Knee Surgery Sports Traumatology Arthroscopy. 2017 Jan;25(1):192-9.

89. Grindem H, Snyder-Mackler L, Moksnes H, Engebretsen L, Risberg MA. Simple decision rules can reduce reinjury risk by 84% after ACL reconstruction: the Delaware-Oslo ACL cohort study. Br J Sports Med. 2016 Jul;50(13):804-8.

90. Herbst E, Hoser C, Hildebrandt C, Raschner C, Hepperger C, Pointner H, et al. Functional assessments for decision-making regarding return to sports following ACL reconstruction. Part II: clinical application of a new test battery. Knee Surgery Sports Traumatology Arthroscopy. 2015 May;23(5):1283-91.

91. Kyritsis P, Bahr R, Landreau P, Miladi R, Witvrouw E. Likelihood of ACL graft rupture: not meeting six clinical discharge criteria before return to sport is associated with a four times greater risk of rupture. Br J Sports Med. 2016 Aug;50(15):946-51.

92. Rambaud AJM, Semay B, Samozino P, Morin JB, Testa R, Philippot R, et al. Criteria for Return to Sport after Anterior Cruciate Ligament reconstruction with lower reinjury risk (CR'STAL study): protocol for a prospective observational study in France. BMJ Open. 2017 Jun 30;7(6):e015087.

93. van der Horst N, van de Hoef S, Reurink G, Huisstede B, Backx F. Return to Play After Hamstring Injuries: A Qualitative Systematic Review of Definitions and Criteria. Sports Med. 2016 Jun;46(6):899-912.

94. Hickey JT, Timmins RG, Maniar N, Williams MD, Opar DA. Criteria for Progressing Rehabilitation and Determining Return-to-Play Clearance Following Hamstring Strain Injury: A Systematic Review. Sports Med. 2017 Jul;47(7):1375-87.

95. Mendiguchia J, Martinez-Ruiz E, Edouard P, Morin JB, Martinez-Martinez F, Idoate F, et al. A Multifactorial, Criteria-based Progressive Algorithm for Hamstring Injury Treatment. Med Sci Sports Exerc. 2017 Jul;49(7):1482-92.

96. Shrier I, Serner A, Wangensteen A, Steele RJ, Weir A. Measuring heterogeneity of reinjury risk assessments at the time of clearance to return to play: A feasibility study. J Sci Med Sport. 2017 Mar;20(3):255-60.

97. van der Horst N, Backx F, Goedhart EA, Huisstede BM. Return to play after hamstring injuries in football (soccer): a worldwide Delphi procedure regarding definition, medical criteria and decision-making. Br J Sports Med. 2017 Nov;51(22):1583-91.

98. Zambaldi M, Beasley I, Rushton A. Return to play criteria after hamstring muscle injury in professional football: a Delphi consensus study. Br J Sports Med. 2017 Aug;51(16):1221-6.

99. Smith M, Vicenzino B, Bahr R, Bandholm T, Cooke R, Mendonça L, et al. Establishing return to play criteria after acute lateral ankle sprain injuries: An international Delphi study. Journal of science and medicine in sport. 2019;22:S108-S9.

100. Bittencourt NFN, Meeuwisse WH, Mendonca LD, Nettel-Aguirre A, Ocarino JM, Fonseca ST. Complex systems approach for sports injuries: moving from risk factor identification to injury pattern recognition-narrative review and new concept. Br J Sports Med. 2016 Nov;50(21):1309- 14.

101. Fonseca ST, Souza TR, Verhagen E, van Emmerik R, Bittencourt NFN, Mendonça LDM, et al. Sports Injury Forecasting and Complexity: A Synergetic Approach. Sports Med. 2020 Oct;50(10):1757-70.

102. Rommers N, RÖssler R, Verhagen E, Vandecasteele F, Verstockt S, Vaeyens R, et al. A Machine Learning Approach to Assess Injury Risk in Elite Youth Football Players. Med Sci Sports Exerc. 2020 Aug;52(8):1745-51.

103. Edouard P, Verhagen E, Navarro L. Machine learning analyses can be of interest to estimate the risk of injury in sports injury and rehabilitation. Ann Phys Rehabil Med. 2020 Aug 29.

104. Needle AR, Lepley AS, Grooms DR. Central nervous system adaptation after ligamentous injury: a summary of theories, evidence, and clinical interpretation. Sports Med. 2017 Jul;47(7):1271-88.

105. Ward S, Pearce AJ, Pietrosimone B, Bennell K, Clark R, Bryant AL. Neuromuscular deficits after peripheral joint injury: a neurophysiological hypothesis. Muscle & nerve. 2015 Mar;51(3):327-32.

Summary

Regular physical activity has beneficial health effects, but simultaneously a considerable risk of incurring a musculoskeletal injury exists. These injuries have substantial repercussions both in the short-term and long-term. Clinicians attempt to mitigate the injury risk by trying to identify people at risk and providing preventative strategies. Injury risk screenings encompass functional performance tests to map impairments that could lead to a future injury. Functional performance tests are measures of physical capacity of an individual involving multi-joint movements or postures. The flaws of the current functional performance tests evidence that a clear need to research the clinimetric properties of current functional performance tests, but also to develop and validate new functional performance tests.

When an individual gets injured, the goal of the clinician will be to improve the patient's quality of life, to let the individual successfully return to sport, to mitigate re-injury risk, and to prevent long-term sequelae. Functional performance tests are also deemed essential within the return to sport decision-making process. Yet, these are generally the same functional performance tests that are used for injury risk screening. Hence, they have identical flaws. Furthermore, the return to sport world consensus statement indicated that "return to sport decisions should always use information gathered from a battery of tests mimicking the reactive elements and the decision-making steps athletes use in real sport situations." Nevertheless, the current functional performance tests do not approach the actual sport context. A similar call for the development and validation of new functional performance tests emerges in the return to sport domain. This is important, since a clear choice was made preferring an objective criteria-based return to sport approach. However, information is lacking on scientifically sound return to sport criteria following common sport injuries. Therefore, research and consensus is needed on return to sport criteria for highly prevalent sport injuries.

In order to bridge the gap between research and clinical practice, the field of sport medicine showed increased interest in the complexity sciences' paradigm. Correspondingly, the application and interpretation of functional performance tests are affected by this. Functional performance tests are thus only one piece of the puzzle when compiling an injury risk profile, monitoring rehabilitation progress, or making a return to sport decision. This also allows for functional performance testing in different contexts with parameters closely related to the sport (e.g. fatigue). Yet when it comes to fatigue research, all too often clinicians have to extrapolate fundamental research findings and make elaborated assumptions in clinical practice. Meaning that the inclusion of various measuring instruments (e.g. psychological, physiological, social, biomechanical) could prove interesting for them. Nevertheless, the functional performance test domain is lacking research on the application of relevant contextual factors. For instance, how different types of fatigue affect functional test performance and alter underlying physiological and psychological mechanisms.

The overall purpose of this dissertation was to contribute to clinical decision-making and functional performance testing across the sport injury spectrum. The three specific objectives encompassed: (1) establishing return to sport criteria following lateral ankle sprains, (2) mapping the reliability characteristics of the reactive balance test, (3) exploring electrophysiological brain changes induced by various types of fatigue when participants performed the Y-balance test and reactive balance test.

The systematic review **(Chapter 2)** showed that currently no scientifically sound return to sport criteria following lateral ankle sprain injury can be determined. This was because not one original research study was performed on this topic. Therefore, we provided an overview of the relevant retrieved questionnaires, clinical assessment measures, functional and sport-specific performance tests within ankle sprain populations. Based upon this empirical research, return to sport variables were proposed. This chapter also encompasses rationales and considerations for return to sport decision-making following lateral ankle sprain injury. For instance, we advocate for the implementation of complex systems theory into return to sport decision-making and the utilisation of the return to sport continuum.

In **Chapter 3**, the reliability study is the first study to assess test-retest, intra- and inter-rater reliability of the reactive balance test within a recreationally trained population. Excellent intra- and inter-rater reliability for both outcomes (i.e. visuomotor response time and accuracy) were found. When having a choice, preferably let the same rater evaluate the outcome measures of the reactive balance test, since the values show marginally better results for intra-rater reliability compared to inter-rater reliability. However, test-retest reliability showed good reliability for visuomotor response time and moderate reliability for accuracy. These results indicate that the reactive balance test is suited for performing analyses over time at the group level.

In the subsequent phase of the project (**Chapter 4 & 5**), the aim was to contribute to the lack of application of contextual factors and need for translational research. This research vacuum was addressed by inducing different types of fatigue in healthy individuals performing the Y-balance test and the reactive balance test, while simultaneously exploring (electro)physiological changes at the brain level.

The third study (**Chapter 4**) was designed to evaluate the impact of mental fatigue on electrophysiological brain measurements during Y-balance test and reactive balance test performance. Even though mental fatigue was successfully induced, it did not affect Y-balance test performance. However, an increase in prefrontal cortex theta activity was observed when performing the Y-balance test in a mentally fatigued state. Which means mental fatigue was successfully induced, and might suggest a lower availability of attentional resources and poorer decision-making. Regarding reactive balance test performance, only accuracy was compromised due to mental fatigue. No changes in visuomotor reaction time and electrophysiological brain outcome measures were found following the mental fatigue intervention.

In **Chapter 5**, the results showed that acute physical fatigue impairs the accuracy of the reactive balance test, while Y-balance test performance and visuomotor response time of the reactive balance test remained unaffected. Nevertheless, the underlying changes at the peripheral and central physiological level completely differed from the previous study. During the execution of both tests, acute physical fatigue induced alterations in electrophysiological brain outcome measures in line with previous Wingate literature. Higher α power in the prefrontal cortex, motor cortex and posterior parietal cortex as well as higher β power in the prefrontal and posterior parietal cortex were observed during the execution of the Y-balance test in a fatigued state. Following acute physical fatigue, α and β power increments were found in the posterior parietal cortex and the prefrontal cortex during the execution of the reactive balance test, respectively.

In summary, the research findings of this dissertation show that:

(1) no scientifically sound return to sport criteria following lateral ankle sprain injury are currently available;

(2) the reactive balance test has acceptable reliability characteristics and therefore is suited for performing analyses over time at the group level.

(3) mental and acute physical fatigue do not impact YBT performance, even when underlying physiological and psychological changes are present;

(4) the reactive balance test is capable of detecting fatigue changes at the group level culminating in decreased accuracy. When mentally fatigued, no changes at the electrophysiological brain level were measured. In a physically fatigued state the electrophysiological findings were partially in line with previous Wingate literature.

A first area for future research is the development of objective return to sport criteria following common sport injuries. Also, a high need exists for more collaboration within the sport injury domain with practitioners, experts in other domains, between research institutes, etc. Research involving neurocognitive functional performance tests could offer innovative ways to assess patients and participants within injury prevention, rehabilitation and return to sport decision-making contexts. An additional research avenue might be to apply relevant contextual factors to bring functional performance testing closer to the relevant sport context. It is necessary to acknowledge that fundamental and translational research are still very much needed and still have an important role to play in the sports injury domain. For instance, the brain is gradually claiming the centre of attention in ligament injury research caused by sports participation. These insights open up perspectives for fundamental, translational and practical research, and could change the way we screen, test, rehabilitate and train these individuals.

Samenvatting

Regelmatige fysieke activiteit heeft gunstige gevolgen voor de gezondheid, maar tegelijkertijd bestaat er een aanzienlijk risico op het oplopen van een musculoskeletale blessure. Deze blessures hebben aanzienlijke gevolgen op zowel korte als lange termijn. Zorgverstrekkers trachten het risico op blessures te verkleinen door mensen met een verhoogd letselrisico te identificeren en preventieve strategieën aan te bieden. Screening van het letselrisico omvat functionele prestatietesten om beperkingen in kaart te brengen die tot een toekomstige blessure zouden kunnen leiden. Functionele prestatietesten zijn een maat voor de fysieke capaciteit van een individu waarbij verschillende gewrichtsbewegingen of houdingen worden uitgevoerd. Rekening houdend met de tekortkomingen van de huidige functionele prestatietesten is er een duidelijke behoefte om de klinimetrische eigenschappen van de huidige functionele prestatietesten te onderzoeken, maar ook om nieuwe functionele prestatietesten te ontwikkelen en te valideren.

Wanneer een individu geblesseerd raakt, is het doel van de clinicus de levenskwaliteit van de patiënt te verbeteren, het individu met succes te laten terugkeren naar de sport, het risico op wederkerende blessures te beperken, en sequelae op lange termijn te voorkomen. Functionele prestatietesten worden ook essentieel geacht in het besluitvormingsproces bij terugkeer naar de sport. Toch zijn dit over het algemeen dezelfde functionele prestatietesten die worden gebruikt voor screening van het blessurerisico, en beschikken dus over dezelfde tekortkomingen. Bovendien stelde de internationale consensusverklaring betreffende het terugkeren naar de sport dat "beslissingen over het terugkeren naar de sport altijd informatie moeten gebruiken die is verzameld uit testbatterijen die elementen nabootsen die atleten in echte sportsituaties ervaren". Niet verwonderlijk benaderen de huidige functionele prestatietesten deze werkelijke sportcontext niet. Een soortgelijke oproep om de ontwikkeling en validatie van nieuwe functionele prestatietesten doet zich dus voor in dit domein. Dit is belangrijk, aangezien er nood is aan een objectieve, op criteria gebaseerde aanpak van de terugkeer naar de sport beslissing. Daarnaast ontbreekt het ons echter aan informatie omtrent wetenschappelijk onderbouwde criteria voor het terugkeren naar de sport na veel voorkomende sportblessures. Daarom is hierover ook onderzoek en consensus nodig.

Om de kloof tussen onderzoek en klinische praktijk te overbruggen, is er op het gebied van de sportgeneeskunde steeds meer belangstelling voor het paradigma van de complexiteitswetenschappen. Ook de toepassing en interpretatie van functionele prestatietesten worden hierdoor beïnvloed. Functionele prestatietesten zijn dus slechts één stukje van de puzzel bij het samenstellen van een blessurerisicoprofiel, het monitoren van de revalidatievoortgang, of het nemen van een beslissing over de terugkeer naar de sport. Zo kunnen functionele prestatietesten ook in verschillende contexten worden uitgevoerd met parameters die nauw verband houden met de sport (bv. vermoeidheid). Maar als het gaat om onderzoek naar vermoeidheid, moeten clinici maar al te vaak fundamentele onderzoeksresultaten extrapoleren en in de klinische praktijk verregaande aannames doen. Dit betekent dat het toepassen van verschillende meetinstrumenten (bv. psychologisch, fysiologisch, sociaal, biomechanisch) tijdens praktisch gericht onderzoek voor hen interessant zou kunnen zijn. Niettemin ontbreekt het in het domein van functionele prestatietesten aan onderzoek naar de toepassing van relevante contextuele factoren. Bijvoorbeeld hoe verschillende soorten vermoeidheid de functionele testprestaties beïnvloeden en ook hoe de onderliggende fysiologische en psychologische mechanismen daar een rol in spelen.

Het algemene doel van dit proefschrift was bij te dragen aan de klinische besluitvorming en het domein van de functionele prestatietesten. De drie specifieke doelstellingen omvatten: (1) het bepalen van terugkeer naar sport criteria na laterale enkelverstuikingen, (2) het in kaart brengen van de betrouwbaarheid van de reactieve balanstest, (3) het onderzoeken van elektrofysiologische breinveranderingen geïnduceerd door verschillende soorten vermoeidheid wanneer deelnemers de Y-balans test en reactieve balanstest uitvoeren.

Uit de systematische review (**Hoofdstuk 2**) bleek dat er momenteel geen wetenschappelijk onderbouwde criteria voor terugkeer naar de sport na een laterale enkelverstuiking beschikbaar zijn. Dit komt doordat er niet één prospectief onderzoek is gedaan naar dit onderwerp. Daarom hebben we een overzicht gegeven van de relevante gevonden vragenlijsten, klinische testen, functionele en sportspecifieke prestatietesten binnen populaties met een enkelverstuiking. Gebaseerd op dit empirisch onderzoek werden terugkeer naar de sport variabelen voorgesteld. Dit hoofdstuk bevat ook argumenten en overwegingen omtrent de besluitvorming in zake de terugkeer naar sport na een laterale enkelverstuiking. Zo pleiten we ook voor de implementatie van de complexe systeemtheorie in de besluitvorming over terugkeer naar de sport en voor het gebruik van het continuüm van terugkeer naar de sport.

De betrouwbaarheidsstudie in **Hoofdstuk 3** is de eerste studie die de test-hertest, intra- en inter-beoordelaarsbetrouwbaarheid van de reactieve balanstest binnen een recreatief getrainde populatie beoordeelt. Uitstekende intra- en inter-beoordelaarsbetrouwbaarheid werd voor beide uitkomsten (d.w.z. visuomotorische reactietijd en accuraatheid) gevonden. Wanneer men de keuze heeft, laat men bij voorkeur dezelfde beoordelaar de uitkomstmaten van de reactieve balanstest beoordelen, omdat de waarden iets betere resultaten laten zien voor intra-beoordelaarsbetrouwbaarheid vergeleken met inter-beoordelaarsbetrouwbaarheid. De test-hertest betrouwbaarheid toonde echter een goede betrouwbaarheid voor visuomotorische reactietijd en een matige betrouwbaarheid voor accuraatheid. Deze resultaten geven aan dat deze test geschikt is voor het uitvoeren van analyses over een tijdspanne op groepsniveau.

In de volgende fase van het project (**Hoofdstuk 4 & 5**), wilde ik bijdragen aan het gebrek aan toepassing van contextuele factoren en de behoefte aan translationeel onderzoek. Dit onderzoeksleemte werd aangepakt door het induceren van verschillende soorten vermoeidheid bij gezonde proefpersonen. Deze voerden de Y-balans test en de reactieve balanstest uit, terwijl tegelijkertijd (elektro)fysiologische veranderingen op het niveau van de hersenen werden onderzocht.

De derde studie (**Hoofdstuk 4**) was ontworpen om de invloed van mentale vermoeidheid op elektrofysiologische breinmetingen tijdens de Y-balans test en de reactieve balanstest te evalueren. Hoewel mentale vermoeidheid met succes werd opgewekt, had het geen invloed op de prestaties van de participanten op de Y-balans test. Echter, werd wel een toename in prefrontale cortex theta activiteit waargenomen bij het uitvoeren van de Y-balans test in een mentaal vermoeide toestand. Dit betekent dat mentale vermoeidheid met succes werd opgewekt, en zou kunnen wijzen op een lagere beschikbaarheid van concentratie en slechtere besluitvorming. Wat betreft de reactieve balansprestatie, werd alleen de uitkomstmaat "accuraatheid" aangetast als gevolg van mentale vermoeidheid. Er werden geen veranderingen gevonden in visuomotorische reactietijd en breinuitkomstmaten na de mentale vermoeidheidsinterventie.

In **Hoofdstuk 5** toonden de resultaten aan dat acute fysieke vermoeidheid de accuraatheid van de reactieve balanstest nadelig beïnvloedt, terwijl de Y-balans testprestatie en de visuomotorische reactietijd van de reactieve balanstest onaangetast bleven. Niettemin verschilden de onderliggende veranderingen op fysiologisch niveau volledig van de vorige studie. Tijdens de uitvoering van beide testen, induceerde acute fysieke vermoeidheid veranderingen in elektrofysiologische breinuitkomstmaten. Hogere α power in de prefrontale cortex, motorische cortex en posterieure pariëtale cortex, evenals hogere β power in de prefrontale en posterieure pariëtale cortex werden waargenomen tijdens de uitvoering van de Y-balans test in een vermoeide toestand. Na acute fysieke vermoeidheid werden α- en β-powertoenames gevonden in respectievelijk de posterieure pariëtale cortex en de prefrontale cortex tijdens de reactieve balanstest.

Samenvattend tonen de onderzoeksresultaten van dit proefschrift aan dat:

(1) er momenteel geen wetenschappelijk onderbouwde criteria voor terugkeer naar de sport na een laterale enkelverstuiking beschikbaar zijn;
(2) de reactieve balanstest over acceptabele betrouwbaarheid beschikt en daarom geschikt is voor het uitvoeren van analyses over tijd op groepsniveau;
(3) mentale en acute fysieke vermoeidheid hebben geen invloed op de Y-balans testprestaties, zelfs niet wanneer er onderliggende fysiologische en psychologische veranderingen aanwezig zijn;
(4) de reactieve evenwichtstest in staat is om vermoeidheidsveranderingen te detecteren, culminerend in een afname van de accuraatheid. Bij mentale vermoeidheid werden geen veranderingen op elektrofysiologisch hersenniveau gemeten. Bij fysiek vermoeidheid waren de elektrofysiologische bevindingen gedeeltelijk in overeenstemming met eerdere Wingate literatuur.

Een eerste suggestie voor toekomstig onderzoek is de ontwikkeling van objectieve criteria voor de terugkeer naar sport na veel voorkomende sportblessures. Ook bestaat er een grote behoefte aan meer samenwerking binnen het sportblessuredomein met zorgverstrekkers uit de praktijk, experts uit andere wetenschappelijke domeinen, tussen onderzoeksinstituten, enz. Onderzoek naar neurocognitieve functionele prestatietesten zou innovatieve manieren kunnen bieden om proefpersonen te beoordelen binnen de context van blessurepreventie, revalidatie en besluitvorming over terugkeer naar de sport. Hierbij zou het ook interessant kunnen zijn om relevante contextuele factoren toe te passen om functionele prestatietesten dichter bij de sportcontext te brengen. Daarnaast hebben fundamenteel en translationeel onderzoek nog een belangrijke rol te spelen in het domein van de sportblessures. Verder komen de hersenen geleidelijk aan in het middelpunt van de belangstelling te staan bij onderzoek naar ligamentletsels als gevolg van sportdeelname. Deze inzichten openen perspectieven voor toekomstig onderzoek, en kunnen de manier veranderen waarop we deze personen screenen, testen, revalideren en trainen.