# Written evidence submitted by the University of Nottingham

## Sports Related Concussion

***Professor Donal McNally***
Donal McNally is Professor of Bioengineering and Head of the Bioengineering Research Group at the University of Nottingham. He has published more than 180 journal conference papers in the field of biomechanics and has been awarded 8 international and national research prizes. His work is primarily focussed on tissue level biomechanics and injury mechanisms including brain injury, particularly in vulnerable individuals. His research includes computational modelling of head injuries and well as experimental investigation of injury both on the field and in cadaveric studies.

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Mary O'Hanlon is a Sport and Exercise Medicine Physician and Assistant Professor in Sport and Exercise Medicine at the University of Nottingham. Prior to her appointment at the University, Mary served in the Royal Air Force as a Medical Officer and has experience working in the NHS. Her current clinical and research interests are in Sports Related Concussion, particularly in the student population and female athletes. Mary leads a specialist Concussion Clinic based in the Department of Sport which supports the diagnosis and rehabilitation of Sports Related Concussion primarily in students but also to the wider community in Nottingham. The Concussion Clinic also provides an educational programme to health and care students and the University sports teams.

**Reason for evidence submission**

We write to highlight the gaps in knowledge and understanding of the pathophysiology and current epidemiology of Sports Related Concussion. Specifically, we emphasise how these impact on the ability to recognise, diagnose and support individuals with Sports Related Concussion not just in elite sport but in the general UK population. Finally, we offer recommendations in 3 broad categories: improving injury surveillance, improving understanding of injury mechanisms and physiology, improving our response to the condition at a population level.

***Introduction***

The health benefits of physical activity and sporting participation are well documented in the general population. We know that elite athletes have long-term health benefits because of their lifetime of being physically active and this includes lower cardiovascular disease and diabetes.[1] However, the recent paper from Dr William Stewart and colleagues has found an increased risk of dementia in retired Scottish Football (Soccer) players.[2]

There is a long association with head injuries and future poor neurological health. Dementia pugilistica, 'punch drunk dementia', has been well documented in combat sports such as boxing and martial arts. The terminology has now evolved to Sports Related Concussion (SRC) but as clinicians it is difficult to clearly define SRC as athletes can have a myriad of symptoms and clinical findings. The 5th Consensus Statement on Concussion in Sport recommended:

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[1] Mary E. Jones, Madeleine A.M. Davies et al: Osteoarthritis and other long-term health conditions in former elite cricketers, Journal of Science and Medicine in Sport 2017.
[2] Daniel F. Mackay, Emma R. Russell et al: Neurodegenerative Disease Mortality among Former Professional Soccer Players, The New England Journal of Medicine 2019.

*'SRC is a traumatic brain injury that is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces with several common features that help defining its nature'.*

Further elaboration in the consensus offered that SRC represents the immediate and transient symptoms of traumatic brain injury (TBI). This recognises that many cases of SRC are short lived. However, it does not give any indication of the underlying pathology and potential impact that SRC can have on the athlete. Furthermore, for some athletes the onset of symptoms is delayed and may evolve over time.

Clearly other sports involving repetitive traumatic head injuries carry a similar risk and this has been highlighted as a possible risk factor in the disease Chronic Traumatic Encephalopathy (CTE). In recent years, there has been high profile interest and research into CTE particularly in National Football League (NFL) players in the USA. It is not clear the volume or force of trauma required to induce CTE and at present, this disease can only be confirmed on post-mortem.

The common factor in all these athletes is that they share a history of repetitive head injuries as part of their training and professional careers. It is difficult to collect robust research data on the link between repetitive head injuries and SRC as it would be unethical to purposefully induce these head injuries and there is a long lag time to neurodegenerative disease such as dementia and CTE. So, it is fair to accept on a balance of high probability that repetitive head injuries are the putative factor.

Current SRC research and its long-term risk is often focussed on elite athletes. However, semi-professional athletes and other enthusiastic exercisers are not routinely involved in data collection and research. It is reasonable to argue that they do not have the same training and performance demands as an elite athlete but due to high participation numbers, they warrant inclusion in future investigation and research. Furthermore, females are frequently not included in research and current published literature is heavily focussed on male participants.

***Pathophysiology***

Sports Related Concussion starts with a mechanical insult to the brain either due to direct head impact or transmission of lower body impacts via the neck. The brain tissue is accelerated rapidly generating forces and deformations within the brain tissue itself. In high energy head injury, such deformations lead to fracture of the skull and brain tissue with rupture of blood vessels leading to haemorrhage and swelling. In SRC, the effects are much more subtle and difficult to detect using current imaging modalities.

The structure of the brain is complex, with sharp transitions between different types of tissues and also the normal fluid filled spaces within the brain. This complexity makes it impossible to generalise local brain mechanics from gross measurements of head motion. Similarly, the heterogenous structure leads to localised areas of loading at the interfaces.

It is clearly unethical to induce SRC experimentally in human volunteers, and measurements, for example head mounted accelerometers, can only give information about motion of the head as a single unit. Whilst animal studies have been used to study concussion, their use is controversial and difficult to place into context. In SRC, the loading of the brain tissue comes from the distribution of mass within the brain under the impact acceleration. Rodents and other experimental animals (including most primates) have brains of very different size, mass and shape making the internal loading of brain tissue, even under comparable mechanical insults, quite different to an equivalent human experiment.

To understand the internal, tissue level mechanics of SRC, we need sophisticated computational models of the head, and particularly the brain, that reflect its complex structure. Such models are starting to be

developed for studying automotive head injuries, but these are focussed on the high energy injuries that are characteristic of road traffic collisions and the observable mechanical failure that results. Similarly, they are limited to adult, usually male, heads and brains that are quite different in mass distribution and material properties to those of children. Models that are relevant to SRC are currently unavailable.

We are still not clear on the underlying pathophysiology and neurobiological effects of SRC and the related deformation of brain tissue. Several hypotheses have been proposed as to how this trauma imparts dysfunction but research to confirm these suggestions are often limited to rodent and other animal studies.

The Lateral Fluid Percussion (LFP) model has proposed concussive forces drives cerebral fluid against the outermost layers of the brain and some specialised imaging techniques have shown changes in cerebral blood flow patterns which may help support this theory.

Another suggestion is that the trauma force to brain is thought to stretch the axons in the brain causing a disruption to the surrounding physiological function and instigates a neurometabolic cascade and hypermetabolism. This initiates the release of neurotransmitters inducing neuronal depression, lactic acid production resulting in further neuronal damage. Calcium release during this dysfunction accumulates and damages the cytoskeleton of the axon and results in histopathological findings of diffuse axonal injury (DAI).

These proposed changes in brain function are thought to resolve over time but there is suggestion that free radical production during this process leads to delayed cell death and an altered metabolic environment and neuroinflammatory response. The effect this has on later neuronal health is not fully elucidated, but we do see neuroinflammation in Alzheimer's disease and depressive episodes. This may explain the later poor neurobiological health in individuals with repetitive head injuries.

Therefore, we need to invest more research into developing sophisticated models of the human brain during SRC, exploring alternative imaging modalities to detect SRC and explore the role of neuroinflammation in SRC and later poor neuronal health.

***Epidemiology***

It is difficult to accurately estimate the incidence of SRC both globally and in the UK and there are many factors to this. It is important to note that concussion can be sustained through accidents and trauma in everyday life and not just through sporting endeavours and is also commonly seen in military service. This may influence the data collected about concussion resulting in data not specific to SRC only.

Sports related concussion is considered part of the spectrum of traumatic brain injuries (TBI) and is sometimes classified as a mild TBI or mild head injury. It is important to emphasise SRC as a TBI as this helps impart the seriousness of the condition. However, the overlapping terminologies, varying definitions and different collection methods globally make collecting and collating reliable data troublesome.

It is widely known that SRC can be poorly recognised by individuals and some medical professionals not experienced in the management of SRC. It is common that individuals with SRC do not report their condition for fear of being withdrawn from sporting participation, the condition is not of a serious nature that they feel warrants medical attention or do they do not have access to medical care to diagnose and manage SRC. Considering these points alone, it is likely that the burden of SRC is heavily underestimated.[3]

[3] Kam Lun Hon, Alexander K.C. Leung and Alcy R. Torres: Concussion - A Global Perspective, Seminars in Neurology 2019.

Looking at trends in recent decades there appears to be an increase in SRC but this likely due to increased awareness of the condition, improved recognition and diagnosis and an increase in sporting participation especially amongst adolescents. Previous estimates have suggested 1.6-3.8 million SRC cases per year in the USA alone and has been termed 'a silent epidemic'.

The greatest incidence appears to be adolescents and young adults, and this may be due to their immature physical and neurological systems, naive sporting technique or simply due to increased sporting participation numbers of these age groups.

There are established risk factors for SRC and also for persisting concussive symptoms. These include learning disabilities such as dyslexia and ADHD, previous concussions and head injuries, migraine disorders, and psychological conditions such as depression and anxiety. We are not currently clear how these risk factors lead to an increase in SRC or prolonged recovery. It is important to note that these risk factors have been deduced from largely male participants in research and so females may have distinctly different risk factors.

Females have been noted to have a higher incidence of SRC in high school and collegiate athletes with studies reporting two times increased risk of SRC. We have found in our own athletes at the University of Nottingham that females have 1.5 increased risk of sustaining SRC. It is not clear why female athletes may be at greater risk for SRC and there is a dearth of literature investigating this higher incidence. Suggestions have included the role of oestrogen levels and other key sex hormones and altered biomechanics in females but so far studies have been inconclusive.

The incidence of SRC in UK is not collected in a coherent manner at this present time. Individual National Governing Bodies (NGB's) and sporting clubs may collect this data but again this is focussed on elite athletes. Data collected by The RFU found 20% of injuries in the professional men's game was attributable to SRC, 19% in the professional women's game and University super league, 25% in youth games and 17% in community rugby.

For semi-professional athletes or the general population, their SRC injury information may only be collected if they attend the Emergency Department or their General Practitioner but this data is not routinely collated. It is difficult to perform a retrospective analysis of data held on NHS patients and SRC injuries as not all athletes will seek medical attention from the NHS, the data may not be accurately recorded (coded) as a SRC injury and varying terminologies. Going forward we need reliable data from NHS attendances to explore later poor health.

Whilst data from College athletes in the USA has a more robust sports injury data collection through their injury surveillance programme, National Collegiate Athletic Association (NCAA), there is not a similar system in the UK for our students at school or further education. There is a strong emphasis on sporting participation at Further Education Colleges and Universities but SRC incidence is not collected in a collaborative manner, if at all by institutions.

Therefore, considering all these factors, we presently do not have an accurate record of the SRC incidence in the UK.

***Diagnosis and management***

There is currently no definitive diagnostic test to confirm the diagnosis of SRC. Clinicians rely on the clinical symptoms and abnormal clinical findings in the context of a traumatic brain injury. Neuropsychological

assessment may be used in the diagnosis and management of SRC, but this is only affordable to the most elite sporting clubs.

Current conventional brain imaging such as Computerised Tomography (CT) and Magnetic Resonance Imaging (MRI) are not able to detect SRC. Both CT and MRI may be used in the evaluation of SRC to exclude other injuries such intra-cranial haemorrhage or structural injuries like a basal skull fracture. If such investigations are normal, athletes are often told 'it's just concussion' indicating this condition does not have any associated morbidity. There is often no follow up offered in the NHS for a diagnosis of SRC.

A very recent study by Professor Belli and colleagues published in March 2021 has found markers in salvia in male professional rugby players which may have the potential to help support future diagnoses of SRC and is promising.[4]

Suspicion of SRC is key to remove an athlete from further sporting participation until fully evaluated by a healthcare practitioner. This is of particular importance in community and grass roots sport where it is unlikely there will be a dedicated medical team. In this environment there is a heavy reliance on ancillary staff such as coaches, referees, teammates, teachers and maybe families to suspect SRC and remove the athlete from play.

Early recognition and removal from play is key since continued sporting participation is linked to slow recovery from SRC, persisting symptoms, increased risk of musculoskeletal injuries and the rare but fatal diffuse cerebral swelling (second impact syndrome). The symptoms of SRC can clearly have an impact on an athlete's activities of daily living including academia and employment in both elite and recreational athletes. There is also some suggestion of increased mental health disorders such as depression and anxiety, but the association of this relationship is not fully understood at the moment.

The main framework on managing and rehabilitating SRC is a period of cognitive and physical rest until symptoms subside and the gradual re-introduction of physical activity and exercise. There are return to learn and play guidelines to support this process but outside of the elite sporting setting and Sport and Exercise Medicine speciality, these are not widely used. Elite sporting settings can advise and guide their athletes through this process but athletes outside of these settings frequently struggle for guidance at this return to play stage.

In our specialist Concussion Clinic, we can provide athletes and students with diagnosis a of SRC and manage their rehabilitation. The primary aim is to support them during symptom resolution so they can return to their activities of daily living including academic and employment commitments. Once this been achieved, we manage their return to sporting participation irrespective of their competition level.

An important facet to our Concussion Clinic is the provision of SRC education to athletes. There is a heavy emphasis on education especially away from elite sporting settings to increase SRC recognition and support reporting. We know that teenagers and young adults are particularly vulnerable to SRC and subsequent complications and there is a heavy reliance on ancillary staff such as coaches and fellow team mates to recognise SRC.

Students are also less likely to seek medical attention and there is a reluctance to make healthy decisions about returning to play post-injury. Concussion education has an important role in reducing the impact of SRC on students' health, University experience and academic performance and is highlighted as an important strategy to increase SRC knowledge and health seeking behaviours in athletes.

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[4] Valentina Di Pietro, Patrick O'Halloran, Callum N Watson et al: Unique diagnostic signatures of concussion in the saliva of male athletes: the Study of Concussion in Rugby Union through MicroRNAs (SCRUM), British Journal of Sports Medicine 2021.

We also provide this education programme for our undergraduate health and care students including medical, physiotherapy and sport rehabilitation students as SRC is not commonly included on undergraduate curriculum but they are likely to encounter SRC in their future careers as healthcare practitioners. We are fortunate at our University to be able to provide this Concussion Clinic service but are mindful that not all teaching institutions can provide this level of care.

**Recommendations**

Whilst we know that SRC is highly prevalent in all areas and levels of sport, we hold little or no long-term data to evaluate its impact. Similarly, although there is a strong epidemiological link between SRC and long-term degenerative brain disease, our understanding of causality is impaired by a lack of knowledge of the basic mechanics and pathophysiology of the condition. Further, although SRC is diagnosed, managed and reported now in elite sports (often only in male athletes) very little is known about its impact in other important groups such as school and student sports.

Our recommendations therefore fall into 3 groups: improving injury surveillance, improving understanding of injury mechanisms and physiology, improving our response to the condition at a population level rather than the current focus on elite sports.

**Improving injury surveillance**

1. Strong, central collection of SRC injury data collection and injury surveillance: by collecting prospective data on SRC in sport (across all levels) and the general population. Using standardised pitch-side protocols, diagnostic techniques and reporting we will have a more accurate understanding of the scale of the problem.
   **We recommend a national register where National Governing Bodies undertake responsibility for data collection.**

2. Standardised recording and coding of SRC injuries and medical attendances to NHS services including General Practice, Emergency Departments and other health and care providers. This will give a more accurate understanding of the scale of the problem in non-elite individuals but also the burden to health and care services.
   **We recommend standardised coding of SRC by the NHS for data collection.**

**Improving understanding of injury mechanisms and physiology**

3. Currently we do not have the diagnostic tools to support recommendations 1 and 2 for anything outside elite sports. Identification of biomarkers, particularly using affordable, saliva-based tests offers the best opportunity for cheap, reliable, sensitive and consistent diagnosis.
   **We therefore recommend support for further research and clinical trials to identify diagnostic markers for SRC.**

4. Removing a concussed athlete from play is only the first step in minimising long-term illness. We also need clear indications of when it is safe to return to training and play.
   **We recommend further research into using the biomarkers and test kits (identified in Recommendation 3) for managing the safe return of individuals to sporting participation.**

5. Whilst SRC is clearly initiated by a mechanical insult to the brain, we understand very little of how this translates to mechanical disruption of brain tissue at the level of the micro-circulation and neurones themselves. Without this insight, it is not possible to explore the pathophysiology of the damage using laboratory experiments.

**We recommend support for research that develops sophisticated, tissue level, models of brain mechanics during concussive injury.**

6. The causative link between multiple SRC and long-term degenerative disease has not been established as the physiological response of brain tissue to relevant mechanical insults has not been established. By establishing the cellular response to such insults, we will not only be able to understand their short-term consequences but also identify diagnostic markers (see Recommendation 3) and also understand the progress of neurodegenerative diseases in relation to traumatic head injuries.
   **We recommend support further research to understand the underpinning pathophysiology in SRC.**

**Improving population level response**

7. To date, research has focussed on elite sports, and largely male athletes. As such, it fails to reflect the majority of the burden of both short- and long-term disease in the UK populations.
   **We therefore recommend a much greater focus on school and student populations and on the female population in general.**

8. Without strong, national engagement at all levels of sport, and all levels of medical intervention, any innovation or improvement in surveillance will be fruitless.
   **We therefore recommend a national education programme for grassroots sport and other medical specialities and practitioners, particularly around return to play.**