

Written evidence submitted by Prof. Huw Williams, Dr Adam Reuben,  
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CONCERN (CONCussion Exeter Research Network)

*Submission to inquiry by Department of Culture, Media & Sport, in UK&NI Parliament, into:*

**“Links between sport and long-term brain injury in an inquiry examining concussion in sport”**

25/03/21

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CONCERN and our affiliates engage in clinically relevant research with sports populations in adolescence and young and into later adulthood.

We are interested in prevention, diagnosis, and management of concussion. To use what we know to better manage the risk and effects of concussion in sports - and in other areas of life too. Our group include award winning specialists in research and clinical practice in Traumatic Brain Injury (TBI).

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**Prof Jo Bowtell:** Professor of Exercise Physiology, Nutrition and Metabolism, Sport and Health Sciences, University of Exeter, and Head of BioActivEx Research Group,.

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## SUMMARY

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We are in a better place to identify if, and when, players are injured (e.g. Neurocognitive testing linked to biomarkers (such as MICRO-RNA) Neuroimaging and player passports etc.), and we are at a point for understanding how we can more safely return players to play (and general activity) to reduce risk of PCS and mood/stress disorders. Importantly there needs to be reasonable consideration of risk (e.g. of dementia) that does not – inadvertently lead to over-caution and negative outcomes through expectations of harm.

These advances in neurosciences need to be taken forward as Public Health messages for sports – so that people can engage in them with greater safety and to gain the health and social benefits of sports. This is paramount for younger brains. And with better knowledge for risks and when to retire from – or - change sports - if issues become problematic.

More broadly, advances in Sports Neuroscience may well have substantial implications for the management of TBI in general. From prevention to management and to recovery.

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Mild Traumatic Brain Injury (MTBI) is one the most prevalent forms of injury leading to disability worldwide. It particularly affects children and young people.

“MTBI” and “Concussion” are often treated as if they are synonymous and interchangeable. Some even advocate “dropping” the term concussion for MTBI.

For brevity and clarity we will note that TBI could most readily apply as a term for situations when we know there is evidence of (effectively) permanent changes in brain structure (and consequently function) through some form of impact on the body that involves translation of

forces to (and on) the brain – such as a clash of head in football, a knee to the head in rugby, a punch to the face in boxing, a head to ground in cycling/skateboarding etc.

Concussion could apply to changes in cerebral systems that could signal such an event – with indications of apparent change in level of awareness/consciousness/balance/ etc. These acute symptoms can resolve completely - leaving no MTBI sequelae - although these may remain “hidden” (for now).

There is, therefore, significant controversy in the field of the Neuroscience SRC/MTBI – even of a consensus on what to name “it”. Having noted this lack of clarity, here is substantial advances in the area of late. We note the advances – but controversies - signal a need for research that is systematic, well controlled, and objective, so that we can develop a better picture of what the issues are.

We note, importantly, the brain is not an organ that is a steady state. There are age and sex based factors that may also contribute to injury and recovery. Vially, there are sensitive periods in the evolution of the connectome. With outcomes being, in general, potentially worse, if injury occurs at times of development.

The key areas we wish to comment on are below:

1. Are there modifiable aspects of play/activity (e.g. rugby/football) that could lessen risk of SRC/MTBI?
  - a. There are **modifiable aspects of play that are linked to SRC/MTBI**. For example, 25% of SRC/MTBI in rugby are the result of foul play – which can be prevented through enforcement of rules and/or and new rules.
  - b. Also SRC/MTBI is **much more common at amateur and school level** rugby than at professional levels due to various factors (e.g. awareness/surveillance) which could be addressed.
    - i. Gardner, A. J., Iverson, G. L., **Williams, W. H.**, Baker, S., & Stanwell, P. (2014). A systematic review and meta-analysis of concussion in Rugby Union. *Sports Medicine*, 44(12), 1717-1731. doi:[10.1007/s40279-014-0233-3](https://doi.org/10.1007/s40279-014-0233-3)
2. Are there age related risk period for worse outcomes?
  - a. **Adolescence/young adulthood appears to be associated with worse outcomes – particularly when concussions are cumulative. People may be less able to pay attention and concentrate effectively, and may be more impulsive.**
    - i. **Wall, S.E., Williams, W. H.**, Cartwright-Hatton, S., Kelly, T. P., Murray, M., Murray, J & Turner, M. (2006). Neuropsychological dysfunction following repeat concussion in jockeys.. *Journal of Neurology Neurosurgery & Psychiatry*, 77(4), 518-520. doi:[10.1136/jnnp.2004.061044](https://doi.org/10.1136/jnnp.2004.061044)
3. Are there biomarkers that are showing promise to indicate brain injury?

- a. **There is a very recent breakthrough in establishing biomarkers (MicroRNAs in saliva) that can indicate a very recent concussion.**
    - i. Di Pietro V, O'Halloran P, Watson CN, *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* Published Online First: 23 March 2021. doi: 10.1136/bjsports-2020-103274
  
  - b. **There is ongoing work to develop objective measures of acute deficits in cognitive, visual and motor function that is adding to our understanding of incidence and severity of acute symptoms of SRC/MTBI.**
  
  - c. **There are neuroimaging techniques that can show us if (i) brain structure (by MRI DTI of diffuse white matter tracts) and (ii) coordinated areas of activity of brain systems (by fMRI) may be affected by SRC/MTBI.**
    - i. Gardner, A., Kay-Lambkin, F., Stanwell, P., Donnelly, J., Williams, W. H., Hiles, A., and Jones, D. K. (2012). A systematic review of diffusion tensor imaging findings in sports-related concussion. *Journal of Neurotrauma*, 29(16), 2521-2538. doi:[10.1089/neu.2012.2628](https://doi.org/10.1089/neu.2012.2628)
    - ii. Cook, M. J., Gardner, A. J., Wojtowicz, M., Williams, W.H., Iverson, G. L., Stanwell, P. (2020). Task-related functional magnetic resonance imaging activations in patients with acute and subacute mild traumatic brain injury: A coordinate-based meta-analysis. *NeuroImage: Clinical*, 25.
4. Is there evidence that certain forms of Return to Play/Activity protocols are based on a sound literature (such as Randomised controlled trials)?
- a. **There is data on frequency of injury (and timing, developmentally) and subsequent prognosis, long term, which can inform protocols and advice for individual's affected, family and others (see i). Including Randomised controlled trials - showing supported, graduated, approaches are beneficial (see ii).**
    - i. Gardner, A, Williams H, Potter, S., Ryland, H., Yates, P.J. Tonks, J., & Reuben, A. (2019). Neurocognitive Assessment of mTBI (Traumatic Brain Injury). In *Traumatic Brain Injury: A Clinician's Guide to Diagnosis, Management, and Rehabilitation*. Ed Jack Tsao, MD, D.Phil. Springer New York ISBN 978-3-030-22435
    - ii. Lal A, Kolakowsky-Hayner SA, Ghajar J, Balamane M. The Effect of Physical Exercise After a Concussion: A Systematic Review and Meta-analysis. *The American Journal of Sports Medicine*. 2018;46 (3):743-752. doi:[10.1177/0363546517706137](https://doi.org/10.1177/0363546517706137)

5. Are there are treatments for managing persistent symptoms of SRC/MTBI months and years later –

a. **Cognitive Behavioural approaches are showing very promising signs of reducing disability see:**

i. Nigel S. King & Alice Coates (2021): Mixed messages from the 'Mild Traumatic Brain Injury' and 'Sport-related Concussion' literatures: Clinical implications, Brain Injury, DOI: 10.1080/02699052.2021.1890216 To link to this article: <https://doi.org/10.1080/02699052.2021.1890216>

b. **Nutritional approaches have potential to support recovery from brain injury.**

Evidence to date is largely based on animal studies and more high quality human trials are required to confirm. Candidate therapeutic nutritional approaches include: omega 3 fatty acids, antioxidants (N-acetyl cysteine, polyphenols), as well as pre- and pro-biotics to correct gut dysbiosis. We have shown in healthy older adults the potential for polyphenols to enhance perfusion and cognitive function **Bowtell JL, Aboo-Bakkar Z et al (2017): Enhanced task-related brain activation and restign perfusion in healthy older adults after chronic blueberry supplementation, Appl Physio Nutr Metab 42: 773-9, DOI: 10.1139/apnm-2016-0550.**

6. Is SRC/MTBI associated with dementia?

a. There is **some evidence that SRC/MTBI MAY be associated with dementia.**

However, there are various forms of dementia. **TBI is associated with a huge array of disorders and social issues (depression, anxiety, alcohol issues, chronic pain, loss of work, relational breaks, violence etc.) - these may be the mediators of outcome** (i.e. be the causal mechanisms for poorer brain health).

b. There is a specific form of dementia suggested to be associated with SRC/MTBI – this being Chronic (and/or) Traumatic Encephalopathy (CTE). **The evidence is, however, not compelling, for SRC/MTBI to be causally linked to CTE.** The hypothesis that CTE results from SRC/MTBI (or putative sub-concussive blows) is based largely on case series investigations and studies with limitations in research methodology. There are calls for improved, well controlled, studies.

i. Willer, B.S., Mohammad, N.D., Wilber, C., Esopenko, C, Turner, M and Leddy, J. (2020) Long-Term Neurocognitive, Mental Health Consequences of Contact Sports. Clinics in Sports Medicine, ISSN: 0278-5919, Vol: 40, Issue: 1, Page: 173-18

c. Furthermore, **the anxiety caused by fears over issues such as CTE have emerged as concerns leading to poorer functioning and mental health problems** in survivors of MTBI. This has become a focus for CBT for Persistent Post Concussion Symptom issues.

i. Nigel S. King (2019) 'Mild Traumatic Brain Injury' and 'Sport-related Concussion': Different languages and mixed messages?, *Brain Injury*, 33:12, 1556-1563, DOI: 10.1080/02699052.2019.1655794 To link to this article: <https://doi.org/10.1080/02699052.2019.1655794>

### Contributors:

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He is a Clinical Psychologist & Clinical Neuropsychologist in Stroke, Neurorehabilitation, Neuro-Disability, Primary Care & Neuropsychological Rehabilitation (Oliver Zangwill Centre). He has given advice to a number of national (e.g. Ministry of Justice) and international (e.g., UNESCO, UN Office for Drugs and Crime) agencies and provided evidence to Parliamentary bodies (Justice Committee UK & NI Parliament & Justice Committee of the Scottish Parliament). In 2019 he was awarded a Fellowship of the BPS and the Barbara Wilson Award for Lifetime Achievement in Clinical Neuropsychology. Dr Huw Williams is an Assoc. Professor in Clinical Neuropsychology. He is on the **Board of Directors** International Concussion and Head Injury Research Foundation (ICHIRF). He has held grants from MRC, ESRC & Barrow Cadbury Trust and authored around a hundred publications – mostly in TBI and PTSD, Brain Development & Neuropsychology, Sports and Crime.

**Dr Adam Reuben:** Consultant in Emergency Care & Medical team of Exeter Chiefs); Lead Clinician, CONCERN; University of Exeter, UK.

A consultant in emergency medicine at the Royal Devon and Exeter hospital and has been club doctor for the Exeter Chiefs for 15 years. A wealth of experience managing elite rugby players with suspected or confirmed concussion, Dr Reuben runs a sports concussion clinic for athletes at the University of Exeter. In addition, he has presented on the subject at local, regional, national and international meetings. Dr Reuben has been a key member of the EMPRESC collaborative, a research collaborative between the departments of Emergency Medicine, psychology and the University of Exeter with a number of successful research projects. Dr Reuben has a track record in academic emergency medicine, having been Chief Investigator and Principal Investigator on a number of portfolio studies including being lead applicant for an NIHR RfPB grant. Dr Reuben is the regional academic lead for the Royal College of Emergency Medicine and has 20 publications in peer reviewed journals.

### **Dr Michael Turner:**

Dr Michael Turner is Medical Director and CEO of The International Concussion and Head Injury Research Foundation (ICHIRF) and Honorary Clinical Associate Professor at University College London (UCL). His former substantive posts include - Chief Medical Adviser (CMA) to the Lawn Tennis Association (1994-2017), CMA to British Horseracing (1992-2013), CMA to the British Ski and Snowboard Federation (1975-2000) and membership of the Medical Committees of FIS, the ITF and European Horseracing. He was a member of the WADA TUE Expert Group (2014-2018), Deputy Director and Director of Medical Services at the British

Olympic Association (1989-1994) and Team GB Medical Officer at the Calgary 1988, Albertville 1992 and Lillehammer 1994 Winter Olympic Games. He is co-author of the Concussion in Sport Consensus Statements from Zurich 2012 and Berlin 2016, and on the expert panel for Paris 2021. His main areas of interest include safety in high- risk sports, protective equipment in sport, concussion and anti-doping.

**Dr Nigel King., University of Oxford, UK**

Dr Nigel King is a Consultant Clinical Neuropsychologist specialising in head injury and trauma. He is the Head of Department of Clinical Neuropsychology at the Community Head Injury Service, Aylesbury, and was a Fellow of Harris Manchester College - University of Oxford from 2008 to 2018. At OXICPT he is a Clinical Tutor. He has published widely in internationally refereed journals in neuropsychology, head injury and post-traumatic stress disorder and is a regular speaker at national and international conferences on these subjects. His self-help book *Overcoming Mild Traumatic Brain Injury* was shortlisted for the British Medical Association Book of the Year Award in their Popular Medicine category. In addition to Dr King's NHS work he regularly acts as an expert witness conducting medico legal assessments for solicitors acting for claimants and defendants, and as a single-joint expert.

**Dr Bert Bond, Ph.D., University of Exeter, UK.**

Dr Bert Bond, PhD. Dr Bert Bond is a lecturer within Sport and Health Sciences at the University of Exeter and co-Director of the Exeter Head Impacts, Brain Injury and Trauma (ExHIBIT) group. His area of expertise includes assessing cerebrovascular health and regulation in different populations, with a particular focus on head impacts in sport. This work is characterising the acute and chronic cerebrovascular alterations to head impacts, which may have relevance regarding the progression of neurodegenerative diseases.

**Dr Genevieve Williams, Ph.D., University of Exeter, UK.**

Dr Genevieve Williams is a lecturer in biomechanics and motor control within Sport and Health Sciences at the University of Exeter and co-Director of the Exeter Head Impacts, Brain Injury and Trauma (ExHIBIT) group. She is developing quantitative pitchside tests to identify and track symptoms of MTBI. She specialises in quantifying human movement and underpinning forces associated with performance and disease and is working on an epistemological shift towards understanding the nonlinear dynamics characteristics of movements to better understand the **bio** aspects of biomechanics. Dr G Williams has received funding from the NIHR Brain injury MedTech Cooperative to support this work.

**Prof. Anthony Belli, University of Birmingham, UK.**

Prof Belli currently is: Professor of Trauma Neurosurgery at University of Birmingham and Honorary Consultant Neurosurgeon at University Hospitals Birmingham. Furthermore he is: Director of NIHR Surgical Reconstruction and Microbiology Research Centre (Trauma Research); Theme Lead of the NIHR Healthcare Technology Cooperative on Trauma

Management; Member of the Leadership Committee for Trauma and Critical Care of the European Association of Neurosurgical Societies; Independent Member of the Expert Panel on Concussion and Head Injury of the Football Association and Rugby Football Union; Advisor England Cricket Board, British Basketball and GB Rowing; Patron of Headway; Trustee of the Midlands Neuroscience Training and Research Fund; Chair of the Military Committee of the World Federation of Neurosurgical Societies. Fellowships with: Royal College of Surgeons of Glasgow (FRCS); Surgical Neurology (FRCS SN); Faculty of Sport and Exercise Medicine (Ireland). Grants from NIHR, John Moulton Trust, EU, EME, MoD, Drake Foundation and others. He has extensive, impactful, publications in Neuroscience.

**Prof. Andrew Gardner, Ph.D.,** *University of Newcastle, NSW, Australia*

Associate Professor Andrew J. Gardner is a Research Fellow at the Priority Research Centre for Stroke and Brain Injury, the School of Medicine and Public Health at the University of Newcastle, and the Hunter Medical Research Institute (Australia). He is also the co-Director of the Hunter new England Local Health District Sports Concussion Clinic. He is a clinical neuropsychologist with a particular interest in sports concussion. His research interests cover the full spectrum of concussion, from injury prevention with tackle techniques, to injury identification via video analysis, to acute assessment through the validation of various measures, to the evaluation of later-in-life brain and mental health of retired athletes. The translational focus of these research programs aims to advance knowledge and improve health care by generating evidence-informed data to advance policy development.

**Prof. Jo Bowtell, PhD,** *University of Exeter, UK*

Jo Bowtell is Professor of Exercise Physiology, Nutrition and Metabolism, where after 5 years as Head of the Sport and Health Sciences Department she is now Associate Dean of Global for the College of Life and Environmental Sciences. Jo's research focus is on exercise and nutrient-induced changes in human physiology and metabolism, especially the effects of polyphenol supplementation on exercise performance and recovery, as well as their potential to support healthy aging of the musculoskeletal and vascular systems. Her group are, for instance, exploring the effects of fruit derived polyphenols on exercise performance, muscle damage and recovery; as well as peripheral and cerebro-vascular function and cognitive function.