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Diagnosis and pathology of sport concussion

Submission date
22/01/2018

Recruitment status
No longer recruiting

Registration date
16/05/2018

Overall study status
Ongoing

Last Edited
27/03/2025

Condition category
Injury, Occupational Diseases, Poisoning

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Sport concussion is as a brief period of loss of consciousness, memory loss or feeling dazed or confused following trauma to the head. It is a common cause of traumatic brain injury (TBI). The aim of this study is to assess the relationship between brain imaging techniques (e.g. MRI scan), blood, saliva and urine biomarkers, and neurophysiological tests in assessing the duration and extent of the window of brain metabolic vulnerability following single and repetitive concussion.

Who can participate?
Athletes and patients aged 16-65 who have sustained either a single or multiple concussions, and uninjured players or players who have sustained musculoskeletal injuries only

What does the study involve?
At the start of the study non-concussed athletes undergo the same tests as for the concussed players, although these may not include MRI scans in all cases due to resources constraints. Pre-season screening assessments will be conducted at either the University Birmingham (UoB) site or the Queen Elizabeth Hospital Birmingham (QEHB) site or at the club facilities. One sample of saliva and one sample of urine are obtained from non-concussed athletes pre-season and after matches; a blood sample may be obtained from non-concussed athletes shortly after. Concussed participants provide a sample of saliva and urine immediately after concussion and their symptoms are assessed. After injury, concussed participants visit QEHB or the UoB or dedicated sport club facilities. Assessments are repeated during the follow up and when the player is deemed fit to return to work/study, or until normalisation of the MRI findings or symptoms. The tests include neurophysiological tests, motor dexterity tests, balance assessments, brain scans (e.g. an MRI scan), and analysis of blood, saliva and urine samples.

What are the possible benefits and risks of participating?
This study will help to identify tests that can support clinical decision making at the pitch-side and in the clinic in order to diagnose concussion, determine the severity of the injury, guide a safe return to play and predict the long-term effects. There are no significant risks to participants, as this is an observational study.

Where is the study run from?
1. Queen Elizabeth Hospital (Heritage Building) (UK)
2. University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
July 2017 to July 2022

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
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Type(s)
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
33971

Study information

Scientific Title
An investigation into Repetitive Concussion in Sport (RECOS)

Acronym
RECOS

Study objectives
Sport concussion, defined as a brief period of loss of consciousness, memory loss or feeling dazed or confused following trauma to the head, is a common cause of traumatic brain injury (TBI). The aim of this study is to analyse the correlation between MR Spectroscopy (1H-MRS), functional MRI (fMRI), Magnetic Resonance Elastography (MRE), functional Near-Infrared

Spectroscopy (fNIRS), blood, saliva and urine biomarkers and neuropsychometric parameters in assessing the duration and extent of the window of brain metabolic vulnerability following single and repetitive concussion.

Objectives:
1. To ascertain the extent and nature of the metabolic and physiological window of vulnerability present in cerebral tissue following mild traumatic brain injury (mTBI) sustained during sport
2. To determine the relationship between a single concussion and subsequent/consecutive episodes in terms of their effect on that window of brain vulnerability with a view to guiding return to play following single and repetitive concussion
3. To intercorrelate biomarkers and neuroimaging with neurophysiological, neuropsychomotor and physiological tests for the prospective development of pitch-side and ambulatory technologies

Ethics approval required
Old ethics approval format

Ethics approval(s)
Essex REC, 22/09/2017, REC ref: 17/EE/0275; IRAS: 216703

Study design
Observational; Design type: Cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Sport concussion

Interventions
Consented non-concussed athletes will participate in a baseline screening consisting of same tests as for the concussed players, although these may not include Magnetic Resonance Imaging (MRI) screening in all subjects due to resources constraints. The uninjured cohort provides normative data, as well as internal control data if a screened player later suffers a concussion during the season. Pre-season screening assessments will be conducted at either the University Birmingham (UoB) site or the Queen Elizabeth Hospital Birmingham (QEHB) site or at the club facilities. The decision regarding the screening location will depend upon the facilities available, the club and convenience for the participants. One sample of saliva and one sample of urine will be obtained from consented non-concussed athletes pre-season and after matches; a blood

sample may be obtained from consented non-concussed athletes shortly after. These samples will be considered as part of the baseline screening and used as control data of the biomarkers level. These samples will be obtained within sport club facilities.
Consented concussed participants will provide a sample of saliva and urine within sport club facilities immediately after concussion. The SCAT5 may be taken within the sport club facilities immediately after concussion. After injury, concussed participants will visit QEHB or the UoB or dedicated sport club facilities where all the assessments will be completed until normalisation of findings.

These assessments will be repeated in the QEHB during the follow up and when the individual is deemed fit to return to work/study, until normalisation of the MR findings or self-reported symptoms are observed.

The following tests which will be undertaken:
1. SCAT5
The Sport Concussion Assessment Tool 5th Edition (SCAT5) will be used to evaluate injured individuals for concussion. The SCAT5 will provide an evaluation of self-reported symptoms and a brief cognitive and physical assessment. This will be conducted by a trained member of the RECOS team or by enhanced care team present at the sport club. It will take around 15 minutes to be completed.
2. Battery of neurophysiological tests
The immediate post-concussion assessment of cognitive testing (ImPACT) is a computerised neurocognitive test used for evaluating sport-related concussion. It measures multiple aspects of cognitive functioning, and consists of five testing composites, i.e. Verbal Memory, Visual Memory, Processing Speed, Reaction Time, and Impulse Control.
The ImPACT will be administrated as per standardized procedures, and test scores from the five composites will be calculated.
The Wechsler Adult Intelligence Scale Version 4 (WAIS-IV) test is designed to measure adults' intellectual function. Two tests of psychomotor speed (Digital Symbol Coding and Symbol Search) will be administered.
Participants may be tested with a Medical Symptom Validity Test (MSVT). The MSVT is a validated and computerized performance validity test. The test is designed to assess the degree to which the participant has engaged appropriately in the testing process.
All the neurophysiological tests described could be given while participants are tested with a non-invasive functional Near-Infrared Spectroscopy (fNIRS).
Prior to any female participants undergoing MR imaging, they will test for B-HCG (pregnancy test) after the expressed consent of the individual.
3. Battery of motor dexterity tests
Tests will include fine motor skill assessments such as the Nine Hole Peg test, whereby the individual will be asked to place and remove nine pegs at one time, as quickly as possible, from none holes in a peg board. This test evaluates coordination of whole upper limbs and hand dexterity.
4. Metabolic/functional scanning
MR scanning will be performed using a 3T MR scanner at the QEHB, which will assess neuronal energy metabolism and functional brain networks. Diffusion Tensor Imaging (DTI) data will also be acquired to reveal brain connectivity in terms of white matter fibre structures. Magnetic Resonance Elastography (MRE) on brain will be performed to obtain quantitative values for tissue mechanical parameters. A map of the tissue stiffness will be acquired through MR images of the induced waves.
5. Serum, saliva and urine metabolomics analysis
One sample of urine and one of saliva will be collected at baseline and after a match of the participants recruited in the study. 25ml of venous blood, which will be drawn by a trained

member of the RECOS team or by enhanced care team present at the sport club, will be drawn immediately after a match from selected participants recruited in the study.
Urine and saliva samples +/- 25ml of venous blood, which will be drawn by a trained member of the RECOS team or by enhanced care team present at the sport club, for metabolomics and genomic analysis will be taken in case of head injury immediately after the trauma.
Consent to obtain these saliva, urine and blood samples will be received during the baseline screening.
New samples of urine and saliva +/- 25ml of venous blood, which will be drawn by a trained member of the RECOS team, for metabolomics and genomic analysis will be taken during the visits of the patients in the Concussion Clinic Birmingham or within dedicated facilities of the participant sports club.
These samples will be sent to the laboratories in the University of Birmingham and in the University Hospital Birmingham NHS Foundation Trust.
6. Battery of balance assessments
A Virtual Reality based balance assessment will be performed with individuals standing on a balance board to measure centre of pressure changes whilst being perturbed in a virtual reality environment. Sufficient safety measures will be put in place to ensure participants do not fall from the raised platform. Gait analysis will be also undertaken.
A balance error scoring system (BESS) test will also be performed whereby a trained member of the RECOS team will assess the number of errors participants make whilst undertaking eyes closed dual, single leg and a tandem stances for 30 seconds respectively.
7. Functional Near-Infrared Spectroscopy
The Near-Infrared Spectroscopy (NIRS) is a safe non-invasive brain imaging technique that utilises Near-Infrared (NIR) light absorption to assess brain oxygen saturation. The NIR light is currently widely used in clinical practice (e.g. pulse oximeter and brain monitoring during cardiac surgery). Participants will be tested with a functional Near-Infrared Spectroscopy (fNIRS) during their first assessment after concussion and during their follow up. During these experiments, the participant will perform neurocognitive and physical tasks. Participants may be tested with an fNIRS during the neurophysiological tests in the baseline screening. We aim to better understand the changes in the brain activation after brain injury.
8. Self-report measures and questionnaires
A Metabolic Equivalent of Tasks (MET) questionnaire will be used to assess participants' physical activity levels prior to the sustaining of a concussion.
Height and weight measurements will be taken in order to calculate BMI.

Intervention Type
Other

Primary outcome measure
1. Saliva and urine biomarkers measured by metabolomic and genomic analysis of samples collected pre-season and at various time points after concussion
2. In addition, some athletes complete a battery of neurophysiological tests (ImPACT, WAIS-IV, MSVT), balance assessments, MRI (1H-MRS, fMRI, MRE, DTI) and blood sampling at 48-72h after injury

All primary analyses will be made according to the matched groups (concussion, uninjured controls and orthopaedic controls). The primary comparison will focus on differential biomarker levels between concussed players and uninjured post-game controls. Unless otherwise specified, estimates of differences between groups will be presented with 95%, two-sided confidence intervals. P-values will be reported from two-sided tests at the 5% significance level. The primary results will be reported after all matches in the 2017-2018 season have been completed

and all samples have been collected and processed for biomarker analysis. Further analyses will conducted in future seasons.

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
01/07/2017

Completion date
31/07/2026

Eligibility

Key inclusion criteria
1. Male or female athletes participating in sports which involve physical contacts between players through our recruitment contacts in University Sports
2. Male or female patients who have been diagnosed with concussion
3. Individuals aged 16-65 years, with fluent English speaking
4. Single or double mTBI as outlined above less than 72 hours prior to assessment
5. Normal neurological objective examination at the time of enrolment

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 400; UK Sample Size: 400

Key exclusion criteria
1. Individuals who require hospital admission after initial assessment for their TBI
2. Intracranial blood, brain tissue injury, or non-TBI related pathologies on initial CT/MR scan
3. Pregnancy (urine pregnancy test will be performed for confirmation)
4. Any history of neurodegenerative pathology or any recent or ongoing illness affecting the central nervous system (e.g. Parkinson’s, multiple sclerosis, meningitis, epilepsy, neoplasm)
5. History of chronic alcohol or drug abuse
6. Any other sustained injury that requires hospital admission

Date of first enrolment
22/09/2017

Date of final enrolment
31/07/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen Elizabeth Hospital (Heritage Building)
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Study participating centre
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Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The compiled and analysed results will be presented at national and international conferences concerning the care of the traumatically brain injured patient. Results will also be submitted for peer review and publication in the subject journals/literature.

Intention to publish date
30/12/2025

Individual participant data (IPD) sharing plan
Subject to the requirements of legislation, including the Data Protection Act 1998 and the Freedom of Information Act 2000, all information obtained about participants during an investigation is confidential unless otherwise agreed in advance. Confidentiality of data is taken very seriously within the NHS Trust. Subject to the requirements of legislation, including the Data Protection Act, all information obtained about participants during an investigation is confidential unless otherwise agreed in advance. It is the responsibility of Experimenters who transfer any MR data out of the NHS Trust for analysis elsewhere to ensure that confidentiality of the data is maintained. All analysed data arising from the experiments will be kept on NHS servers. The computers on this network have restricted physical access; data are stored under coded filenames and the local network has secure password access restricted to a limited set of

people. The raw MRI data are kept on a separate DICOM server on another network behind its own firewall which is only accessible by a small number of system administrators. Subject score sheet data will be kept on computers with password protected access and coded file names, the original paper files will be secured in locked filing cabinets. The datasets generated during and /or analysed during the current study are/will be available upon request from Professor Antonio Belli, who is the point of contact and will be able to provide anonymised data with sufficient detail to able to reproduce the analyses for up to 10 years.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V3.2	18/07/2017	16/05/2018	No	Yes
Protocol article	protocol	04/07/2019	18/08/2020	Yes	No
Interim results article	Identification of salivary microRNAs associated with concussion in male professional rugby players (SCRUM sub-study)	01/12/2021	26/05/2022	Yes	No
HRA research summary			28/06/2023	No	No
Interim results article	Developing a multivariate model for the prediction of concussion recovery in sportspeople: a machine learning approach	24/03/2025	27/03/2025	Yes	No