ISRCTN18210449 https://doi.org/10.1186/ISRCTN18210449

Mild traumatic brain injury biomarker study, a prospective cohort biomarker study of military and civilian participants with mild traumatic brain injury

Submission date
13/04/2023

Recruitment status
Recruiting

Registration date
21/08/2023

Overall study status
Ongoing

Last Edited
07/10/2025

Condition category
Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol

Background and study aims
There are over a million hospital visits each year in the UK for mild traumatic brain injury (mTBI), sometimes called concussion. Although it is classed as mild, a third of patients can't work a year after their injury; it leads to a disproportionate impact on future health. Mild traumatic brain injury can be caused by physical impact to the head through accident, injury or sport, or due to the effects on the brain of shockwaves caused by explosions.
The consequences of mTBI are profound, with many patients suffering long-term disability due to persistent headaches, imbalance, memory disturbance and poor mental health. We can't yet identify those most at risk of these disabling consequences. This is a clear unmet need which would allow the targeting of treatments to improve patient outcomes. The main aim of this study is to develop a predictive biomarker model for outcomes after mTBI.

Who can participate?
Patients aged between 18 and 60 years (inclusive) with confirmed mild traumatic brain injury within the last 3 months can participate in the main study.
Any member of the public aged between 18 and 60 years (inclusive) without confirmed mild traumatic brain injury can participate in the case-control and biological variability substudies.

What does the study involve?
The mTBI participants will have in-person assessments (clinical and imaging) at baseline (both 21 days and 3 months after mTBI), with remote follow-up continuing until 2 years after mTBI. 40 mTBI participants will repeat either the baseline clinical assessments or baseline imaging assessments 4 times within 12 days, as part of the biological variability sub-study.
Patients can be recruited at three points after injury: 0-24 hours post-injury, 21 days post-injury, or 3 months post-injury. The total number of visits will vary depending on the point of study entry.
The first 40 healthy volunteers will repeat either all clinical assessments four times within 12 days, or all imaging assessments six times within 19 days, as part of the biological variability sub-

study. The remaining healthy volunteers will have a baseline (clinical and imaging assessment) and limited remote follow-up for 3 months.
All baseline (21-day and 3-month) assessments, whether clinical or imaging, will be the same for mTBI participants and healthy volunteers.

What are the possible benefits and risks of participating?
For mTBI patients, there is the potential that they will receive a more in-depth post-injury follow-up than would normally be the case. Otherwise, there is not expected to be any direct benefit.
As there is no intervention involved in this study the risks are considered minimal. There is a risk of adverse effects related to the study procedures:
1. Bruising from taking blood samples
2. Discomfort/feeling of claustrophobia from MRI scanners
3. Feelings of nausea from vestibular assessment

Where is the study run from?
University of Birmingham Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
September 2021 to November 2029

Who is funding the study?
Ministry of Defence (UK)

Who is the main contact?
Ryan Ottridge and Andy Palmer, mTBI-Predict@bham.ac.uk

Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)

319062

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RG_22-004, IRAS 319062, CPMS 56875

Study information

Scientific Title
Mild traumatic brain injury biomarker study, a prospective cohort biomarker study of military and civilian participants with mild traumatic brain injury (mTBI-Predict)

Acronym
mTBI-Predict

Study objectives
Mild traumatic brain injury (mTBI) (sometimes called concussion) is common with over 1 million hospital visits due to mTBI each year in the UK. Although classed as mild, it leads to a disproportionate impact on future health, with 3 in 10 patients unable to work 12 months after their injury.

This study will test key biomarkers to allow the identification of mTBI patients at risk of long-term health issues. Biomarkers need to be accurate, reproducible and practical to use in a clinical setting.

The researchers will conduct a long-term study following patients after a new mTBI. At the onset, they will measure a variety of different, but complementary biomarkers including brain imaging, brain physiology, blood and saliva, headache, mental health, vision, balance and cognitive performance. The researchers will then look at the ability of these biomarkers to predict long-term complications at 6, 12 and 24 months post-injury. This will allow those with a good prognosis to rapidly return to service/work/play and those likely to suffer complications to receive prompt and targeted therapy.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 09/05/2023, Ministry of Defence Research Ethics Committee (Defence Science and Technology, Dstl Portsdown West, Fareham, PO17 6AD, United Kingdom; +44 (0)300 153 5372; DST-MODRECTeam@mod.gov.uk), ref: 2217/MODREC/23

Study design
Longitudinal prospective cohort study with nested variability and case-control studies in military and civilian populations including impact, blast and sports injury

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Mild traumatic brain injury

Interventions
The 610 mTBI participants will have in-person assessments (clinical and imaging) at baseline (both 21 days and 3 months after mTBI), with remote follow-up continuing until 2 years after mTBI. 40 mTBI participants will repeat either the baseline clinical assessments or baseline imaging assessments 4 times within 12 days, as part of the biological variability sub-study.

Patients can be recruited at three points after injury: 0-24 hours post-injury, 21 days post-injury, or 3 months post-injury. The total number of visits will vary depending on the point of trial entry.

The first 40 healthy controls will repeat either all clinical assessments four times within 12 days, or all imaging assessments six times within 19 days, as part of the biological variability sub-study. The remaining healthy controls will have a baseline (clinical and imaging assessment) and limited remote follow-up for 3 months.

All baseline (21-day and 3-month) assessments, whether clinical or imaging, will be the same for mTBI participants and healthy control volunteers.

Intervention Type
Other

Primary outcome(s)
The ability of candidate biomarkers to predict full return to play, work or duty at 6 months post-injury, measured using:
1. Headache: patient-completed headache diary
2. Mental Health: Post-Traumatic Stress Disorder checklist
3. Vestibular: vestibular perceptual thresholds
4. Cognition: Corrected Global Composite Score
5. Visual: retinal nerve fibre layer thickness
6. Imaging: MRI, magnetoencephalography (MEG)
7. Hormone/biofluids: cortisol, glial fibrillary acidic protein
8. Cerebral physiology: cerebrovascular reactivity, physical function tests

Key secondary outcome(s))
The ability of candidate biomarkers to predict global function, persistent post-traumatic headache, cognitive dysfunction, depression, PTSD, vestibular disturbances and physical function at 6 months, measured using:
1. Headache: patient-completed headache diary
2. Mental Health: Post-Traumatic Stress Disorder checklist
3. Vestibular: vestibular perceptual thresholds
4. Cognition: Corrected Global Composite Score
5. Visual: retinal nerve fibre layer thickness
6. Imaging: MRI, magnetoencephalography (MEG)
7. Hormone/biofluids: cortisol, glial fibrillary acidic protein
8. Cerebral physiology: cerebrovascular reactivity, physical function tests

Exploratory outcomes:
Accuracy of a multifaceted computer-modelled biomarker algorithm to predict sequelae of mTBI (full return to play, work or duty, persistent post-traumatic headache, cognitive dysfunction, depression, PTSD, vestibular disturbances, and physical function) using computer modelling at 6 months post-injury

Completion date
30/11/2029

Eligibility

Key inclusion criteria
Main study:
1. Aged ≥18 and ≤60 years
2. mTBI: acute (<3 months) mild traumatic brain injury (as per VA/DoD criteria)

Healthy controls:
1. Aged ≥18 years and ≤60 years
2. Healthy (screened through NHS General Health Questionnaire)

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Key exclusion criteria
Main study:
1. Prior diagnosis of PTSD or severe mental illness (e.g. bipolar disorder or psychosis)
2. Pregnancy
3. Prior brain injury (from trauma, stroke or other aetiologies) without full functional and symptomatic recovery
4. Inability to comply with study schedule or follow-up
5. Inability to provide informed consent (e.g. due to cognitive impairment)
6. Any progressive neurodegenerative or neuroinflammatory condition
7. Alcohol use disorder or drug dependence
8. Patients with medical conditions that are unstable or untreated

Healthy controls:
1. Medical condition requiring treatment or significant past medical history
2. Prior diagnosis of PTSD or severe mental illness
3. Pregnancy
4. Prior brain injury (from trauma, stroke or other aetiologies) without full functional and symptomatic recovery
5. Inability to comply with study schedule or follow-up
6. Inability to provide informed consent (e.g. due to cognitive impairment)
7. Inability to safely enter the MRI environment (for imaging variability and case-control study)
8. Any progressive neurodegenerative or neuroinflammatory condition
9. Cardiovascular or cerebrovascular disease or hypertension (no current diagnosis/medication)
10. Alcohol use disorder or drug dependence
11. Patients with medical conditions that are unstable or untreated
12. History of pituitary hormone deficits

Date of first enrolment
01/06/2023

Date of final enrolment
31/05/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
University of Nottingham
University Park
Nottingham
United Kingdom
NG7 2RD

Study participating centre

Aston University
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United Kingdom
B4 7ET

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Ministry of Defence

Alternative Name(s)
MOD

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes