

# A study to investigate the prevalence of pituitary gland dysfunction and its risk factors following traumatic brain injuries (TBI)

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 14/09/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 20/05/2021	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

The number of patients that are hospitalised or that die as a result of traumatic brain injury (TBI) is between 150 to 250 patients per 100,000 population per year. In Scotland this equates to 7,500 patients per year. Up to one third of these patients have long-term problems with their pituitary gland (a gland that regulates vital body function and hormones) function (also known as post TBI pituitary dysfunction or PTPD). This would make PTPD by far the commonest cause of hypopituitarism (when the pituitary gland fails to produce enough hormones). The pituitary gland sits at underneath the brain, where it is surrounded by bones of the skull base. It is therefore susceptible to damage during TBI as it may be injured by the surrounding bones. The pituitary gland is a key part of the endocrine system. The endocrine system is important for maintaining metabolism but also has key roles in regulating stress, energy, libido, bone and muscle strength. It also involved in regulating mental health and wellbeing. Pituitary hormone dysfunction is therefore a serious illness that can cause physical and neuropsychiatric disabilities that can affect the way people recover following TBI. PTPD can be reversed if diagnosed early treatment and an effective screening programme for diagnosing the patients most at risk could represent one of the most important interventions in the management of patient with TBI in the last few decades. The aim of this study is to investigate how common is pituitary dysfunction following traumatic brain injury (TBI).

### Who can participate?

Patients aged 17 and older who have a primary TBI.

### What does the study involve?

Participants undergo blood tests to assess their pituitary gland function one week, within the first month, between three and six months and between six and 12 months after TBI. Participants are checked for their hormones levels at the first stage of the study. During this first stage, 20 participants receive an MRI (a scan using magnetics) of their brain. During the follow up stages, participants also have tests to assess their levels of growth hormone

deficiencies (GHD) and secondary hypoadrenism (SH). During the third and fourth stages of follow up, participants are asked to fill out questionnaires to assess their recovery following a TBI.

What are the possible benefits and risks of participating?  
Not provided at time of registration.

Where is the study run from?

1. Western General Hospital (UK)
2. Royal Infirmary of Edinburgh (UK)

When is the study starting and how long is it expected to run for?  
September 2016 to August 2020

Who is funding the study?  
Edinburgh and Lothians Health Foundation (UK)

Who is the main contact?  
Dr John Emelifeonwu

## Contact information

### Type(s)

Public

### Contact name

Dr John Emelifeonwu

### Contact details

Bramwell Dott Building  
Western General Hospital  
Crewe Road South  
Edinburgh  
United Kingdom  
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## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

2017/0146

## Study information

Scientific Title

# Pituitary gland deficiencies after traumatic brain injury: An Outcomes and Prevalence Study

## Acronym

PitSTOP

## Study objectives

Post-traumatic brain injury (anterior) pituitary gland dysfunction (PTPD) is common following traumatic brain injury and clinical and radiological factors at the time of trauma may predict the risk of developing long-term PTPD.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

South East Scotland Regional Ethics Committee 02, 18/07/2017, ref: 17/SS/0043

## Study design

Multi-centre cross-sectional longitudinal cohort study

## Primary study design

Observational

## Secondary study design

Cross sectional study

## Study setting(s)

Hospital

## Study type(s)

Diagnostic

## Participant information sheet

See additional files

## Health condition(s) or problem(s) studied

Traumatic brain injury

## Interventions

After informed consent, recruited participants have blood tests to assess the function of their brain. These tests are all performed between 8am and 10am and the patients have to be 'fasted' (nothing to eat from midnight the night before) before the blood test. The blood tests are performed at four stages during follow up:

Stage 1. In the first week after Traumatic brain injury (TBI)

Stage 2. Within the first month after TBI

Stage 3. At six months after TBI

Stage 4. At 12 months after TBI

Baseline levels of the following hormones are checked at all 4 stages. These include tests for: cortisol, insulin-like growth factor 1 (IGF-1), growth hormone (GH), prolactin, sodium, thyroid-stimulation hormone (TSH) and free thyroxine (FT4), testosterone levels in men and oestrogen

levels in premenopausal women who do not have a regular menstrual cycle. All of these blood tests can be performed using 3.5mLs (approximately half a tablespoon) of blood.

Also, during the first stage, a subset of participants will also have an magnetic resonance imaging (MRI) of their brain. These scans will be done at every stage of follow-up and will be done on the same day that the patients have their blood test. The MRI scans will be done to check whether there are any structural changes in the pituitary gland that can help predict likelihood of developing long-term PTPD.

The MRI protocol lasts less than 30 minutes and will include the following sequences: T1-weighted 3-D volumetric sequences of the whole brain T2-weighted 2D sequences of the whole brain 3-D Susceptibility weighted imaging (SWI) sequences of the whole brain T1-weighted and T2-weighted fine slices (2mm) of pituitary gland 30 direction diffusion-tensor imaging (DTI) with axial and sagittal sequences

During the second, third and fourth stages of follow up, in addition to the baseline blood tests, participants also have stimulation tests for growth hormone deficiencies (GHD) and secondary hypoadrenism (SH):

**1. Stimulation test for GHD:**

GHRH + Arginine test is used to test for GHD. During this test, a dose of a hormone called growth hormone release hormone (GHRH) (1 micrograms per Kg) is given with a protein called Arginine ( 30g in 100mLs) as an infusion over 30 minutes. Blood samples to check GH levels are then taken at 30 minutes and at 60 minutes after the start of the infusion.

**2. Stimulation test for SH:**

Short Synacthen test (SST) is used to test for SH. During this test, a sample of blood is taken and then an intramuscular injection (into muscle, usually the shoulder muscle) of Synacthen is given. Synacthen is a synthetic hormone that mimics one of the hormones of the pituitary gland called ACTH. After it has been injected, two further blood tests are done 30 minutes and 60 minutes after the injection to analyse whether the Synacthen has caused an appropriate rise in the level of a hormone called cortisol.

The injections that are given during the stimulation tests are either naturally occurring or synthetic versions of naturally occurring substances. They are tolerated by most patients but the tests are done under the supervision of an appropriate clinician, in case of any adverse reactions.

The patients selected to have an MRI scan at the first stage have the scan repeated at all follow ups stages. Finally, during the third and fourth stages, participants are asked to complete the extended Glasgow Outcome Score (GOSE) to assesses functional recovery following TBI.

This feasibility study is planned to test all aspects of the PitSTOP protocol prior to starting the main study. During this feasibility study, the first follow up stage will be omitted.

**Intervention Type**

Biological/Vaccine

**Primary outcome measure**

Prevalence of post TBI pituitary gland dysfunction (PTPD) is measured with pituitary function test (baseline measurements of serum thyroid stimulating hormone, free T4, testosterone, IGF-1

and cortisol) acutely (within 7 days), sub-acutely (within one month) and long-term (up to 6 months and up to 12 months) after TBI. Also a short synacthen test and GHRH + Arginine tests will be performed in the sub-acutely (within one month) and long-term (6 month and 12 months).

### **Secondary outcome measures**

1. Clinical and radiological markers are measured using the clinical information available at the time of presentation to hospital and serial MRI of the pituitary gland performed acutely, within one month and long-term (6 to 12 months) in a subset of patients to try to predict the occurrence of PTPD
2. Optimal timing for surveillance for PTPD using the clinical and radiological information detailed above
3. Functional recovery of patients with PTPD using Glasgow Outcome Score (eGOS) at end of study period (six to 12 months)

### **Overall study start date**

01/09/2016

### **Completion date**

01/08/2020

## **Eligibility**

### **Key inclusion criteria**

1. Primary traumatic Brain Injury (TBI) including multi trauma
2. Patients aged 17 years at the time of TBI
3. Informed consent obtained from participant

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Sex**

Both

### **Target number of participants**

100

### **Key exclusion criteria**

1. Patients with a pre-existing endocrine diagnosis
2. Morbidly obese patients with BMI > 35
3. Unlikely to survive for the next 24 hours in the opinion of the Intensive care or Neurosurgical team treating the patient
4. Patients with known epilepsy
5. Patients on medications that are known to affect the hypothalamic-pituitary axis
6. Patients who are not able to consent

### **Date of first enrolment**

01/12/2017

**Date of final enrolment**

01/12/2019

**Locations****Countries of recruitment**

Scotland

United Kingdom

**Study participating centre****Western General Hospital**

Crewe Road South

Edinburgh

United Kingdom

EH4 2XU

**Study participating centre****Royal Infirmary of Edinburgh**

51 Little France Crescent

Old Dalkeith Road

Edinburgh

United Kingdom

EH16 4SA

**Sponsor information****Organisation**

University of Edinburgh

**Sponsor details**

Academic and Central Clinical Office for Research and Development

College of Medicine & Veterinary Medicine

University of Edinburgh

The Queen's Medical Research Institute

47 Little France Crescent

Edinburgh

Scotland

United Kingdom

EH16 4TJ

**Sponsor type**

University/education

**Website**

<http://www.accord.scot/>

**ROR**

<https://ror.org/01nrxf90>

## Funder(s)

**Funder type**

Charity

**Funder Name**

Edinburgh and Lothians Health Foundation

**Alternative Name(s)**

ELHF

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United Kingdom

## Results and Publications

**Publication and dissemination plan**

We intend to publish the results of this study by February 2020.

**Intention to publish date**

01/02/2020

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are/will be available upon request from John Emelifeonwu ([johnemelifeonwu@gmail.com](mailto:johnemelifeonwu@gmail.com)), Investigator

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No