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Neural mechanisms of movement, balance and spatial orientation in health and disease

Submission date
13/10/2016

Recruitment status
No longer recruiting

Registration date
19/01/2017

Overall study status
Completed

Last Edited
21/09/2023

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The brain is responsible for controlling balance and orientation in the space around us (spatial orientation). This function allows us to effortlessly walk in busy environments such as a crowded pavement or even to get out of bed at night and walk around in the dark. To achieve such effortless balance, the brain uses information from the vestibular (balance system) and auditory (system for the sense of hearing) systems in the inner ear, joint and muscle sensors (that help to control limb movement) and what we see. The brain also uses information from previous experience, such as using memories of the layout of the furniture in a room to navigate when we are unable to see in darkness. This study aims to assess how the brain combines these different signals to help our balance in health and disease.

Who can participate?
Adults with brain injury affecting brain functioning and healthy adults of the same age.

What does the study involve?
Participants are invited to attend three hospital appointments over the course of the study, spaced two-three months apart. At each appointment, participants will be assessed by a doctor to check for any changes in health status such as migraine or new onset dizziness. At the visit, participants may undergo an MRI scan, in order to assess how well the central nervous system (the brain and spinal cord) is functioning. In addition, participants complete a number of clinical and behavioural testing that assess the basic mechanisms of nervous functioning that may affect balance (these tests typically occur while seated and include testing of the functioning - and their brain connections - of the inner ear balance and hearing organs, the eye and limb muscles). Finally, patients undergo formal tests of balance which will take place when standing or walking (for safety, patients are either harnessed or accompanied by a researcher). These tests are then repeated three and six months later.

What are the possible benefits and risks of participating?
There are no direct benefits of participating, although the results will provide valuable information for the future development of effective therapies for patients suffering with imbalance and spatial disorientation. There are no notable risks involved with participating.

Where is the study run from?
1. Charing Cross Hospital (UK)
2. St Mary's Hospital (UK)
3. Hammersmith Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2017 to March 2021

Who is funding the study?
1. Medical Research Council (UK)
2. Imperial College Healthcare Charity (UK)

Who is the main contact?
1. Dr Barry Seemungal (scientific)
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Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1

Study information

Scientific Title
An observational study of the mechanisms contributing to recovery in imbalance and spatial disorientation following injury to the nervous system

Study objectives
Study aims:
1. To investigate how movement, balance and orientation are impaired in conditions that affect the functioning of the brain
2. To help provide a mechanistic explanation for the future development of therapy in neurological patients with impaired balance and spatial orientation

Hypothesis:
Brain networks coordinate human balance function, and disruption of these networks from disease is important in impairing balance and spatial orientation in humans.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Observational prospective case-control study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Balance, dizziness and spatial disorientation

Interventions
At baseline, participants attend a study visit where they undergo neuroimaging using MRI to assess the structural and functional integrity of the central nervous system. This session will take around an hour.

A series of behavioural and neurophysiological tests (i.e. non-invasive measures of the body's and brain's electrical activity and excitability) are also performed either whilst seated or lying down, to assess functions that can affect balance and spatial orientation performance. The tasks include visual, vestibular and auditory stimuli which may require verbal or button press responses. Balance performance will be objectively measured through assessment of body motion during standing and walking tasks. For safety, patients will be tethered or accompanied by a researcher for the standing and walking tests. This testing session will take half a day.

Follow-up will take place at three and six months.

Intervention Type
Other

Primary outcome measure
1. Functional independence is measured using the Functional Independence Measure ('FIM') score at 6 months
2. Cumulative falls over 6 months are measured monthly by reviewing patient diaries either via telephone or by email (or face-to-face during the two follow-up sessions)

Secondary outcome measures
1. Central and peripheral vestibular and ocular motor function is measured at baseline, 3 and 6 months
2. Balance is measured using the Romberg coefficient and measures of sway at baseline, 3 and 6 months
3. Neurophysiological markers of recovery are measured using evoked potential amplitudes and latencies and temporo-spatial changes in electrophysiological spectral power at baseline, 3 and 6 months
4. Imbalance and dizziness symptoms are measured using the DHI (dizziness handicap inventory) at baseline, 3 and 6 months
5. Migraine features are measured using IHS criteria (International Headache Society criteria) at baseline, 3 and 6 months
6. Anxiety is measured using the Generalized Anxiety Questionnaire (GAD-7) at baseline, 3 and 6 months
7. Depression is measured using the Patient Health Questionnaire (PHQ-9) at baseline, 3 and 6 months
8. Cognitive function is measured using the Montreal Cognitive assessment, the Mesulam's Cancellation Test, the Line Bisection Test and the Trail Making Test at baseline, 3 and 6 months
9. Blood markers of inflammation are measured from blood samples collected at baseline, 3 and

6 months
10. White and grey matter and whole brain functional connectivity are measured using MRI scanning at baseline, 3 and 6 months

Overall study start date
01/01/2017

Completion date
01/03/2021

Eligibility

Key inclusion criteria
Patients
1. Injury to the brain and its sensorium (including eyes, ears, proprio-somatosenory system) from trauma, inflammation and/or disturbed vascular supply
2. Age 18-75
3. Male or Female

Controls
1. Healthy individual
2. Age 18-75
3. Male or Female

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
225 (includes patients and controls)

Key exclusion criteria
Patients
1. Premorbid acute or chronic medical condition that might impair balance and/or spatial orientation (e.g. previous peripheral or central vestibular disturbances)
2. Premorbid active psychiatric, neurological or neuro-otological condition
3. Premorbid substance abuse

Controls
1. Chronic medical condition requiring drug therapy (healthy controls with a past history of migraine in remission will be admissible)
2. Premorbid acute or chronic medical condition that might impair balance and/or spatial orientation (e.g. previous peripheral or central vestibular disturbances)
3. Premorbid active psychiatric, neurological or neuro-otological condition
4. Premorbid substance abuse

Date of first enrolment
01/03/2017

Date of final enrolment
01/03/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre
St Mary's Hospital
Praed Street
London
United Kingdom
W2 1NY

Study participating centre
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0HS

Sponsor information

Organisation
Imperial College Healthcare NHS Trust

Sponsor details
Joint Research Compliance Office
Room 21
Medical School
St Mary's Campus
London
England
United Kingdom
W2 1NY

Sponsor type
Hospital/treatment centre

Website
http://www.imperial.nhs.uk/

ROR
https://ror.org/056ffv270

Organisation
Imperial College London

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Joint Research Compliance Office
Room 215
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Sponsor type
University/education

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Imperial College Healthcare Charity

Results and Publications

Publication and dissemination plan
Publications in peer reviewed journals - open access.

Intention to publish date
01/06/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from barseem@gmail.com.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications		14/10/2022	21/09/2023	Yes	No
Results article		15/12/2022	21/09/2023	Yes	No
Results article		01/01/2021	21/09/2023	Yes	No