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Diversity in blood flow control to the brain

Submission date
15/04/2014

Recruitment status
No longer recruiting

Registration date
09/05/2014

Overall study status
Completed

Last Edited
30/10/2020

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
The brain, more than any other organ in the body, requires a constant supply of blood in order to maintain its function. When blood pressure drops, small arteries increase in size to restore flow levels, and when pressure rises, they narrow to protect the most delicate blood vessels and avoid bleeding and swelling in the brain. Failure of this control system (called cerebral autoregulation) following brain injury can lead to worse outcomes, and also influence the management of changes in blood pressure. This study aims to improve methods for measuring cerebral autoregulation and to gain a deeper understanding of the complex relationship between blood pressure and blood flow in healthy individuals as well as in patients following stroke.

Who can participate?
Healthy volunteers and stroke patients (stroke onset less than 24 hours) , aged 18 years or over.

What does the study involve?
Each subject will have up to six assessments in total. Up to four of these will be in the acute stroke phase, up to 72 hours from stroke onset (at 9, 12, 24 and 48 hours, depending on how soon after stroke you were admitted). The last two assessments will carried out in the subacute phase (within 2 weeks) and in the chronic phase (at 3 months after the stroke). For each assessment, the subject will be asked to lie quietly on the bed whilst a small cuff is attached to the fingers of one hand to measure the blood pressure, three stickers to the chest will allow us to monitor the subjects heart rate, and small tubes placed at the base of the nose will allow us to monitor the breathing. The subject will be asked to wear a head-frame, which will hold the small ultrasound probes that are used to measure blood flow to the brain against both sides of the head, and an ultrasound probe (similar to a pen) will be held against the neck (near the chin) to measure the blood flow through the neck. After about 20 minutes the readings will have stabilised, and we will make recordings for 15 minutes: at rest (5 minutes), when breathing a slightly higher but safe concentration of waste gas (5% carbon dioxide) in addition to oxygen via a mask placed over the subjects mouth and nose (5 minutes), and during a period when the subjects arm will be flexed and extended at the elbow on the side of the body affected by the stroke (5 minutes).

What are the possible benefits and risks of participating?
The participant will receive no personal benefit from taking part in this study. The blood

pressure cuff applies only a gentle pressure to your fingers to enable a blood pressure recording to be made every heartbeat. This may cause a slight tingling in your fingers, but this should not be painful or cause any harm. Indeed, this type of blood pressure monitoring is often used routinely in patients under general anaesthetic or in intensive care. The head-frame and ultrasound probes will exert a slight pressure against your head. However, this is not painful, and again is routinely used in many units to monitor blood flow to the brain. For the manoeuvre to breathe in 5% carbon dioxide, a face mask will be placed covering your nose and mouth. Some people find this uncomfortable, but there are no side effects of the carbon dioxide as the concentration being used for the purpose of this study is very low.

Where is the study run from?
The study recruitment and assessments will all take place at Leicester Royal Infirmary (UK)

When is the study starting and how long is it expected to run for?
June 2014 to March 2017

Who is funding the study?
The Engineering and Physical Sciences Research Council (UK)

Who is the main contact?
Prof. Tom Robinson
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
V0.2

Study information

Scientific Title
Diversity in blood flow control to the brain: moving from individualized modelling towards personalized treatment of the injured brain

Study objectives
By quantifying impairments in blood flow and blood pressure control (based on the cerebral autoregulation and Baroreflex systems), would this impact on the management of an individual patients blood pressure in the acute and chronic phases following stroke?

Ethics approval required
Old ethics approval format

Ethics approval(s)
North East - Newcastle & North Tyneside 1 Research Ethics Committee, 07/07/2014, REC ref: 14 /NE/1003

Study design
Prospective observational study

Primary study design
Observational

Secondary study design
Other

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
Acute and chronic stroke

Interventions
Initial assessments will be undertaken in a dedicated cardiovascular research laboratory, which is at a controlled temperature (20-24 degrees celsius) and is free from distraction. Beat-to-beat blood pressure will be recorded continuously using the Finometer cuff device attached to the middle finger of the non-dominant hand (hemiparetic hand in stroke patients). Heart rate will be recorded using a three-lead ECG, and end tidal CO2 (EtCO2) monitored using small nasal cannulae placed at the base of the nose (Salter Labs, ref 4000) attached to a capnograph (Capnocheck Plus) to monitor breathing. Bilateral ultrasound of the middle cerebral arteries (MCA) will be performed using a probe secured in place using a head frame.

In those patients who have not had a carotid scan an ultrasound probe will be held against the neck (near the chin) to visualize the artery in the neck and measure the blood flow through the neck to measure blood flow velocity of the internal carotid arteries (ICA). Also, in those patients in whom the MCA cannot be identified, the ICA will be used as a surrogate location to measure CBF. These parameters will be simultaneously recorded onto a computer software (PHYSIDAS), providing data for subsequent analysis.

After about 20 minutes the readings will have stabilised, and we will make recordings for 15 minutes: at rest (5 minutes), when breathing a slightly higher than normal, but safe, concentration of waste gas (5% carbon dioxide) in addition to oxygen via a mask placed over the mouth and nose (5 minutes), and during a period when the arm will be flexed and extended at the elbow (5 minutes for each arm, repeated twice).

Follow-up assessments: in stroke patients up to five follow-up assessments will be made, up to three of which will be in the acute stroke phase within 72 hours from stroke onset (at 12, 24 and 48 hours, depending on how soon after stroke the patient was admitted and recruited). The last two assessments will be carried out in the subacute phase (within 2 weeks) and in the chronic phase (at 3 months after stroke). At each assessment the protocol outlined above for baseline assessment will be repeated.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
This is not an intervention study, and therefore it would not be appropriate to assess the classical primary and secondary outcome measures such as death and disability for this study. However, we intend to evaluate the following relevant outcomes:

1. The percentage of recruited subjects (acute stroke patients and healthy volunteers) able to comply with the full measurement protocol
2. The percentage of measurements rejected because of aspects related to data quality during the analysis protocol, with recorded reasons
3. Overall, the percentage of recruited subjects (acute stroke patients and healthy volunteers) in whom values for the following parameters can be derived:
3.1. Autoregulation index (using the Tiecks model and from the phase, gain and coherence)
3.2. Baroreceptor Sensitivity index (using power spectral analysis to acquire the á index)
3.3. % change in coronary blood flow velocity at baseline and in response to a hypercapnic and passive motor stimulus
3.4. Indices of dynamic CA, cerebrovascular reactivity and neurovascular coupling

Secondary outcome measures
N/A

Overall study start date
01/06/2014

Completion date
01/03/2017

Eligibility

Key inclusion criteria
1. Participant (or relative of the stroke patient) is willing and able to give informed consent (assent) for participation in the study
2. Male or female, aged 18 years or above
3. Able (in the investigator's opinion) and willing to comply with all study requirements
4. Willing to allow his or her General Practitioner to be notified of participation in the study

Stroke patient-specific inclusion criteria:
1. Clinical diagnosis of stroke within 24 hours of onset (for patients waking with a stroke, time of onset will be taken to be the time when the patient was last asymptomatic)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60

Key exclusion criteria
Co-morbidity with life expectancy less than 3 months

Date of first enrolment
29/09/2014

Date of final enrolment
01/03/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Leicester Royal Infirmary
Infirmary Square
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Sponsor information

Organisation
University of Leicester (UK)

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Sponsor type
University/education

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ROR
https://ror.org/04h699437

Funder(s)

Funder type
Research council

Funder Name
Engineering and Physical Sciences Research Council (UK) (EP/K041207/1)

Alternative Name(s)
UKRI Engineering and Physical Sciences Research Council, Engineering and Physical Sciences Research Council - UKRI, Engineering & Physical Sciences Research Council, EPSRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	white paper	01/04/2016	30/10/2020	Yes	No
Results article	healthy volunteer results	01/09/2016	30/10/2020	Yes	No
Results article	results	11/07/2018	30/10/2020	Yes	No
	results				

Results article		03/09/2019	30/10/2020	Yes	No
Results article	results	01/02/2018	30/10/2020	Yes	No
Results article	results	01/12/2019	30/10/2020	Yes	No
Results article	results	01/09/2020	30/10/2020	Yes	No
Results article	results	17/04/2020	30/10/2020	Yes	No
Results article	results	01/12/2020	30/10/2020	Yes	No
Results article	results	01/11/2017	30/10/2020	Yes	No
Results article	results	01/05/2016	30/10/2020	Yes	No
HRA research summary			28/06/2023	No	No