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B-cells in stroke-associated infection

Submission date	Recruitment status	[ ] Prospectively registered
13/08/2018	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
24/09/2018	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
28/06/2022	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Stroke-associated infection (SAI) is one of the most common complications of stroke, affecting up to one third of patients, and is the biggest factor for predicting the likelihood of significant disability or death. Currently, there are no effective treatments that prevent SAI and improve stroke outcome. Current evidence has found that stroke can impair the body's natural ability to fight infection but the process has never been fully understood. Using laboratory models of stroke, researchers have investigated how having a stroke can affect the cells that make up the body's natural immune system. In healthy people, special immune cells called B cells help the body respond quickly to infection by triggering the production of antibodies, but after stroke this process is interrupted. The aim of this study is to measure to scale of B-cell changes after stroke, and assess the processes involved and the consequences of the changes.

Who can participate?
Patients aged 18 and over who have had a stroke and healthy volunteers

What does the study involve?
Blood samples are taken from stroke patients at 24-48 hours after their stroke began to measure the levels of B cells. Further assessments include alternate daily infection screen on days 1-7 after the stroke. A single blood sample is also taken from healthy volunteers of a similar age and sex.

What are the possible benefits and risks of participating?
There are no expected benefits except participants will be helping to increase the understanding of the impact of stroke on the function of the immune system. Risks include discomfort and bruising as a result of blood sampling, and data protection, as research staff will be required to access the medical notes of the patients and will be storing personal data for a short period of time.

Where is the study run from?
Salford Royal NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
August 2018 to March 2022

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Prof. Craig Smith
craig.smith-2@manchester.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Craig Smith

ORCID ID
https://orcid.org/0000-0002-9078-9919

Contact details
CSB, Salford Royal NHS Foundation Trust
Stott Lane
Salford
United Kingdom
M6 8HD
+44 (0)161 206 0623
craig.smith-2@manchester.ac.uk

Additional identifiers

Protocol serial number
237040

Study information

Scientific Title
Understanding stroke-induced B cell changes and their relationships with stroke-associated infection

Study objectives
Study rationale is to determine the effects of stroke on innate-like B cells (type of immune cell).

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West, 18/07/2018, ref: 18/NW/0415

Primary study design
Observational

Study design
Single-centre prospective observational cohort study

Study type(s)
Other

Health condition(s) or problem(s) studied
Acute stroke

Interventions
Baseline clinical characteristics performed following consent (including past medical history, prior level of independence, current stroke severity (NIHSS), risk factors and swallow status), current antibiotic treatment, standardised Stroke-Associated Infection (SAI) screen based on Centers for Disease Control and Prevention [CDC] criteria (including clinical features and most recent clinical, laboratory and other investigation findings).

Blood samples will be obtained from stroke patient participants at 24-48h post stroke onset and will be measured for B cell subset quantification by flow cytometry and for the isolation of B cells for ex vivo stimulation assays to measure functional responsiveness at the School of Biological Sciences, University of Manchester. In addition, a single blood sample will be obtained and analysed in the same way from non-stroke controls of a similar age and sex. Further research assessments including alternate daily infection screen (day 1-7 post stroke).

Differences in outcome measures between stroke patients and non-stroke controls will be compared using Student's t test or non-parametric equivalent. Anonymised clinical data including incidence of SAI and clinical outcome assessment (telephone assessment of modified Rankin Scale score) will be correlated with concentrations of blood markers assessed by Pearson correlation or non-parametric equivalent.

Added 15/06/2020:
The COVID-19 sub-study will recruit patients with suspected or confirmed COVID-19 infection prior to stroke or complicating current stroke to investigate the effect of stroke on immune susceptibility to infection. Blood sampling at a single timepoint within 7 days of stroke onset will allow immunophenotyping analysis. Sub-study participants will remain in the trial for the same duration of participants in the main trial and undergo alternate daily follow-up during in-patient stay (to a maximum of 7 days from date/time of blood sampling) and telephone follow-up at 3 months to assess recovery using modified Rankin Scale score.

Intervention Type
Other

Primary outcome(s)
1. Numbers and composition of blood B cell subsets and key immune cell classes, measured using flow cytometry at 24-48h post stroke onset in stroke patients
2. Concentration of blood IgM and catecholamines (noradrenaline and adrenaline), measured using multiplex array, ELISA, EIA and HPLC (high-performance liquid chromatography) at 24-48h post stroke onset in stroke patients and in non-stroke controls
3. Functional responsiveness (e.g. antibody secretion) of blood B cells measured by ex vivo stimulation assay at 24-48h post stroke onset in stroke patients and in non-stroke controls

Added 15/06/2020:
4. Immunological characteristics/markers associated with vulnerability to COVID-19 (sub-study participants only) using multiplex array, ELISA, EIA and HPLC (high-performance liquid chromatography) within 7 days post-stroke onset

Key secondary outcome(s)
1. Incidence of Stroke-Associated Infection (SAI) based on Centers for Disease Control and Prevention [CDC] criteria at 3 months
2. Clinical outcome assessed with telephone assessment of modified Rankin Scale score at 3 months

Completion date
20/03/2022

Eligibility

Key inclusion criteria
Stroke patients:
1. Age ≥18 years
2. Clinical diagnosis of middle cerebral artery (MCA) territory ischaemic stroke or haemorrhage stroke (primary intracerebral haemorrhage)
3. NIHSS ≥8
4. Swallowing difficulties identified on swallow screen performed within 24h of stroke admission
5. Capacity to give consent to blood sampling and follow-up OR availability of personal /professional consultee
6. Blood draw can be undertaken 24-48h after stroke onset (or time last seen well)

Non-stroke controls:
Aged over 18

Added 15/06/2020:
COVID-19 sub-study:
1. Age ≥18
2. Clinical diagnosis ischaemic stroke or haemorrhagic stroke (primary intracerebral haemorrhage; ICH) in any cerebral territory
3. Suspected or confirmed diagnosis of COVID-19 (either prior to stroke admission or within 7 days of stroke onset)*
4. NIHSS >2 (regardless of swallow status)
5. Capacity to give consent to participation or verbal declaration from personal consultee prior to blood sampling
6. Blood draw can be undertaken within 7 days of stroke onset (or time last seen well)

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
145

Key exclusion criteria
Stroke patients:
1. Stroke of other aetiology or unclear diagnosis (e.g. traumatic, stroke mimic)
2. Rapidly improving symptoms at the point of screening
3. History of infection treated with antibiotics at admission or in the preceding 6 weeks
4. Unlikely to survive or palliative care considered to be imminent

Non-stroke controls:
1. Previous stroke
2. Infection or antibiotic therapy in previous 6 weeks

Added 15/06/2020:
COVID-19 sub-study:
1. Stroke of other aetiology or unclear diagnosis (e.g. traumatic, stroke mimic)
2. Rapidly improving symptoms at the point of screening
3. Unlikely to survive or palliative care considered to be imminent

Date of first enrolment
06/08/2018

Date of final enrolment
21/06/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Salford Royal NHS Foundation Trust
Stott Lane
Salford
United Kingdom
M6 8HD

Sponsor information

Organisation
Salford Royal NHS Foundation Trust

ROR
https://ror.org/019j78370

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Craig Smith (craig.smith-2@manchester.ac.uk). Consent will be sought from all participants, data is fully anonymised.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No