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Spinal cord area measurement using MRI in monitoring diabetic neuropathy

Submission date
01/03/2021

Recruitment status
No longer recruiting

Registration date
08/04/2021

Overall study status
Completed

Last Edited
21/12/2022

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Diabetic peripheral neuropathy is a type of nerve damage as a result of high blood sugar levels in people with diabetes. The condition causes numbness, reduced ability to feel pain and temperature changes, and tingling sensations. It affects the feet and legs first, followed by the hands and arms, and is often worse at night. A consequence of this condition is that people may not notice injuries due to reduced ability to feel pain, which can lead to wounds becoming infected and ulcers developing.

The purpose of the study is to determine what happens to the spinal cord over time, specifically a reduction in size, in people who have diabetes mellitus with or without problems in the peripheral nerves (peripheral neuropathy) using magnetic resonance imaging (MRI) scans. The study team would like to understand whether a reduction of the spinal cord area over a year is associated with other features of disease progression in diabetic peripheral neuropathy (for example changes in the severity of pain and the threshold of vibration sensation). If a relationship between spinal cord atrophy and disease progression is found, this could be used to screen people with diabetes for peripheral neuropathy or monitor those with diabetic peripheral neuropathy.

This study will compare the findings in people with diabetic peripheral neuropathy to people with diabetes but without peripheral neuropathy and to other groups (healthy volunteers, people with multiple sclerosis, and people with other types of peripheral neuropathies).

Who can participate?
People aged 18 to 75 years old who have either diabetes (with or without peripheral neuropathy), multiple sclerosis, or peripheral neuropathy without diabetes, or do not have any of these conditions can participate in the study. The study will assess all potential participant to make sure it is safe for them to have an MRI scan before including them in the study.

What does the study involve?
Participants will meet a doctor from the research team to discuss participation in the study and make sure there is no reason to exclude them from the study. The first visit will happen at baseline and another follow-up visit will happen 12 to 24 months later.

Participants will be asked to complete some questionnaires about quality of life, anxiety and depression, daily function, and pain. A brief history taking and clinical examination will be performed (20-50 min depending on the underlying condition). Participants will undergo vibration perception threshold testing (5 min), a simple test where a 'neurothesiometer' is put in contact with on the toes and participants are asked to let the researcher know if they can feel the vibration.

Participants will also have some blood tests to assess certain markers of inflammation and metabolism. Some blood will be saved for DNA (genetic) screening to detect common genetic predisposing factors. The DNA portion of the study will be optional. A urine sample will be obtained for protein measurement and validation of some of the markers present in the blood. The samples will be saved in the licenced freezer in the laboratory of Prof Constantinescu under the Human Tissue Act 2004.

Participants will be asked to come to the Sir Peter Mansfield Imaging Centre (SPMIC) at the University of Nottingham for the MRI scans. This will be scheduled at a time that is convenient for the participant. Once at the SPMIC, participants will be asked to complete two brief medical questionnaires before the scan to make sure it is safe for them to have the scan. Participants will be shown the scanner and the researcher will explain beforehand exactly what will happen and the length of time that you will be scanned for. Because the scanner is built around a large magnet, participants will have to remove all metal from your body, including jewellery. Participants may prefer to wear loose non-metallic clothing and/or may be asked to change into clothing provided. Once the session begins, there is an intercom system that will allow participants to communicate with the researcher. Participants may choose to stop at any point if they feel uncomfortable by pressing a buzzer to alert the investigator, who will stop the scanner immediately. The MRI scanner is quite noisy, so participants will be provided ear plugs and ear defenders to wear during the scan. Participants will stay at the imaging centre for approximately 1 h.

All procedures will be repeated at another visit, 12 to 24 months after the first one.

The clinical assessment and sample collections will take place at the Department of Academic Clinical Neurology, Queen's Medical Centre and the MRI scan will take place at the Sir Peter Mansfield Imaging Centre, University of Nottingham. The two centres are close to each other. The study team will arrange for all assessments to take place in one day and can help to arrange transport to and from the centre.

What are the possible benefits and risks of participating?
The study team cannot promise that participating in the study will help participants, but the information from this study may help to care for patients with similar conditions in the future. The study team would like to develop the imaging technique to diagnose spinal cord involvement in diabetes and monitor this over time for any progression.

Participants will have an MRI scan of their spinal cord and brain as part of the study. If the study team find anything unexpected in these scans, participants and their GP will be informed and arrangements will be made for participants to be appropriately assessed depending on the finding.

MRI uses radio waves similar to those used in radio and TV transmission. These have a much lower energy than X-rays and as such are considered biologically safe. The study team will be following strict national safety guidelines which are designed to prevent the potential hazards of MRI which are burns and electric shocks. Preventable accidents like skin burn at the contact

point have never occurred in the participating imaging centre and have only very rarely occurred elsewhere in the UK. Participants will undergo safety questionnaires at the time of the screening, consenting and just prior to scanning to ensure there are no contraindications to them being scanned (including but not restricted to pacemaker, foreign body in the eyes, certain aneurysm clips, and un-removable piercings). During an MRI scan, certain types of tattoos may heat up if they are inside the region being scanned; in exceptional conditions, burning may occur around the tattoo (in extreme cases leading to blistering). For people with facial or genital tattoos or large tattoos (greater than 7.5 cm across), such burning could be inconvenient or uncomfortable and may require medical care. People may feel tingling at the site of the tattoo during scanning; if it heats up, this provides a warning of a potential problem. MRI can also evoke feelings of claustrophobia due to its small size.

Brief mild discomfort and slight bruising are not uncommon due to blood sampling and participants will be warned prior to the procedure. Experienced staff will perform the procedure to minimise this.

Where is the study run from?
Nottingham University Hospitals NHS Trust (UK)

When is the study starting and how long is it expected to run for?
From December 2016 to December 2024

Who is funding the study?
The Nottingham University Hospitals (NUH) Charity (UK)

Who is the main contact?
Prof Nikos Evangelou, Nikos.Evangelou@nottingham.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
209300

Protocol serial number
Sponsor reference 16082, IRAS 209300

Study information

Scientific Title
Spinal Imaging in Neuropathy of Diabetes: Longitudinal Evaluation (SpINDLE)

Acronym
SpINDLE

Study objectives
To determine the longitudinal course of spinal cord atrophy by measuring the spinal cord area at different levels (using magnetic resonance imaging and semi-automatic image analysis methods) over a year in people with diabetic neuropathy and to assess its correlation with clinical and electrophysiological variables.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/03/2017, East Midlands - Leicester Central Research Ethics Committee (Devonshire Place, 78 London Road, Leicester, LE2 0RA, UK; +44 (0)207 104 8388; leicestercentral.rec@hra.nhs.uk), ref: 17/EM/0087

Study design
Single-centre observational cross-sectional and longitudinal case-control study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Spinal cord atrophy in people with diabetic neuropathy

Interventions
There will be 5 study groups:
1. Diabetes without diabetic peripheral neuropathy (DM-DPN)
2. Diabetes with diabetic peripheral neuropathy (DM+DPN)
3. Healthy volunteers (HV)

4. Multiple sclerosis (MS)
5. Other peripheral neuropathies (OPN)

All participants will undergo structural magnetic resonance imaging of the spinal cord and brain and clinical assessment, have their blood and urine samples collected, and complete questionnaires at baseline and at a second timepoint between 12 to 24 months.

Intervention Type
Other

Primary outcome(s)
Upper cervical cord area measured using magnetic resonance imaging at baseline and between 12 and 24 months

Key secondary outcome(s))
1. Lower cervical cord area measured using magnetic resonance imaging at baseline and between 12 and 24 months
2. Mid-thoracic cord area measured using magnetic resonance imaging at baseline and between 12 and 24 months
3. Brain volume measured using magnetic resonance imaging at baseline and between 12 and 24 months
4. Clinical severity of diabetic neuropathy measured using clinical examination, vibration perception threshold, and neuropathic pain scores at baseline and between 12 and 24 months

Completion date
01/12/2024

Eligibility

Key inclusion criteria
1. Aged between 18 and 75 years
2. Able to give informed consent
3. Able to speak and understand English language
4. Diagnosis consistent with one of the study groups (diabetes without diabetic peripheral neuropathy, diabetes with diabetic peripheral neuropathy, healthy volunteers, multiple sclerosis, or other peripheral neuropathies) with initial symptoms having preceded inclusion into the study by 12 months and/or condition stable for ≥2 months

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Key exclusion criteria
1. Extensive cardiovascular and/or cerebrovascular comorbidity (treatment for angina or peripheral vascular disease constitutes a contraindication)
2. Other comorbidities, in particular neurological diseases, that in view of the researcher may interfere with the study
3. Significant spinal or spinal cord disease (other than MS in the MS control group)
4. Contraindications for MRI including but not restricted to pacemaker, orbital foreign body, certain aneurysm clips, claustrophobia, and un-removable piercings
5. Pregnancy or planning for pregnancy

Date of first enrolment
13/03/2019

Date of final enrolment
01/12/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen's Medical Centre
Department of Academic Clinical Neurology
C Floor, South Block
Nottingham University Hospitals NHS Trust
Nottingham
United Kingdom
NG7 2UH

Sponsor information

Organisation
University of Nottingham

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Nottingham University Hospitals NHS Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

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?
HRA research summary			28/06/2023	No	No
Protocol file	version v3.0	19/01/2021	04/05/2021	No	No