

Investigating the effects of nimodipine on spinal reflex measures in humans

Submission date 18/04/2024	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 24/04/2024	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 25/04/2024	Condition category Signs and Symptoms	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

This study investigates the acute effect of a well-known FDA-approved calcium-channel blocker, nimodipine, on transmission in human spinal reflex pathways involving the ratio of the size of the H-reflex to the size of the M-wave (the H/M-ratio) a method of analyzing changes in motoneuron reflex excitability, the cutaneous reflex, and the stretch reflex. This will locate the action site of nimodipine in the human spinal cord, provide indirect evidence of the existence of Persistent Inward Currents (PICs) in humans, and explore the prospect of nimodipine's use in future antispasmodic treatment.

Who can participate?

Healthy, adult volunteers (first part of the project) and adult neurological patients with spasticity both aged 18 years old and over

What does the study involve?

People with muscle stiffness will participate in the study where they won't know if they will receive a real medication or a fake one. On the first day, they will take either nimodipine (60mg) or a chalk tablet (the fake one). Then, they will return on another day to try the other option. A doctor who is not part of the study will keep track of who gets what, and will only disclose who received what after the research team has analysed the results in analysis software.

What are the possible benefits and risks of participating?

There are no personal benefits from participating in the study. The overall goal is to get a better understanding of human motor control and reflex behaviour which are often associated with spasticity.

There are very few risks associated with the measurements used in the study. Nimodipine may cause a temporary drop in blood pressure. Baclofen may cause temporary fatigue or nausea.

Where is the study run from?

Panum Institute in Copenhagen and the Glostrup Hospital (Denmark)

When is the study starting and how long is it expected to run for?
August 2019 to August 2025

Who is funding the study?
1. The Novo Nordisk UK Research Foundation (UK)
2. University of Copenhagen (Denmark)

Who is the main contact?
Eva Rudjord Therkildsen (MD PhD student), ertherkildsen@sund.ku.dk

Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number

514-0849/23-3000

Study information

Scientific Title

Investigating the acute effect of the calcium-channel blocker, nimodipine, on spinal reflex measures in humans

Study objectives

It is hypothesised that the calcium-channel blocker nimodipine will have an acute (~30-90 minutes) effect on spinal reflex measures, hypothetically through inhibition of CaV-mediated persistent inward currents (PICs) in the spinal inter- and motor neurons. Approx. 30-90 minutes after oral tablet intake of nimodipine (Nimotop), this will result in:

1. A decrease in the H/M-ratio
2. A decreased stretch reflex
3. A diminished cutaneous reflex
4. Decreased measures of self-sustained motor neuron firing (e.g., PICs)

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 29/01/2021, The Regional Committee (VEK) - the Capital Region of Denmark (Kongens Vænge 2, Hillerød, 3400, Denmark; +45 38 66 50 00; regionh@regionh.dk), ref: H-20041588

Study design

Double-blind randomized crossover controlled trial

Primary study design

Interventional

Study type(s)

Other

Health condition(s) or problem(s) studied

Healthy individuals and individuals with spasticity

Interventions

Healthy volunteers are involved in a double-blinded placebo-controlled cross-over study. All subjects receive either nimodipine (60mg) or baclofen (25mg) on the first experimental day. All subjects return on a different occasion (at least 24 hours after the first experimental day) to receive the other intervention.

Individuals with spasticity are involved in the double-blinded placebo-controlled cross-over study. All subjects receive either nimodipine (60mg) or a chalk tablet (placebo) on the first experimental day. All subjects return on a different occasion (at least 24 hours after the first experimental day) to receive the other intervention.

An external medical doctor performs the double blinding and will reveal the blinding after all results have been analysed in MatLab.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Nimodipine [Nimotop 60 mg tablet], baclofen [25 mg tablet]

Primary outcome(s)

H/M-ratio measured using surface electromyographic (EMG) analysis of soleus muscle activity before and at 30, 60 and 90 minutes after intervention

Key secondary outcome(s)

The following secondary outcome measures are measures using surface EMG before and at 30, 60 and 90 minutes after the intervention:

1. The size of the stretch reflex during rest and voluntary pre-contraction measured using surface EMG
2. The size of the cutaneous reflex measured using surface EMG from m. tibialis anterior and m. soleus

Completion date

01/08/2025

Eligibility

Key inclusion criteria

1. Age 18 years old and over
2. Adults capable of providing informed consent for participation
3. Healthy volunteers will be recruited in the first part of the project
4. In the second part of the project, individuals with symptoms of muscle overactivity (spasticity /spasms/cramps/dystonia) due to CNS damage are recruited

Participant type(s)

Healthy volunteer, Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Key exclusion criteria

1. Hypotension (systolic blood pressure <100mmHg)
2. Known impaired liver function, cerebral edema, or significantly increased intracranial pressure
3. Antispastic medication that cannot be paused, or recent botox injections

Date of first enrolment

01/02/2023

Date of final enrolment

01/02/2025

Locations

Countries of recruitment

Denmark

Study participating centre

The Panum Institute, Building 33.3

Blegdamsvej 3B

Copenhagen

Denmark

2200

Sponsor information

Organisation

University of Copenhagen

ROR

<https://ror.org/035b05819>

Funder(s)

Funder type

Research organisation

Funder Name

Novo Nordisk UK Research Foundation

Alternative Name(s)

Novo Nordisk UK Research Foundation (NNUKRF), The Novo Nordisk UK Research Foundation, ovo Nordisk Research Foundation UK, NNUKRF

Funding Body Type

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United Kingdom

Funder Name

Københavns Universitet

Alternative Name(s)

university_of_copenhagen, Københavns Universitet - University of Copenhagen, University of Copenhagen (UCPH), Copenhagen University, Københavns Universitet – Københavns Universitet, University of Copenhagen (KU), Denmark, Københavns Universitet – University of Copenhagen (UCPH), koebenhavns_uni, Københavns Uni, University of Copenhagen, KU, UCPH

Funding Body Type

Government organisation

Funding Body Subtype

Universities (academic only)

Location

Denmark

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 Eva Rudjord Therkildsen, ertherkildsen@sund.ku.dk. The datasets are stored in a non-public, secure closed server repository (securefile), specifically for the University of Copenhagen, and RedCap. The data stored on securefile are the EMG data recordings from the experiment. In RedCap information on the type of injury and spasticity are securely stored. Written consent from participants is required and obtained. Data are anonymized (using an ID). The key for the ID is saved on a closed server (the University of Copenhagen). Final data storage plans will be disclosed at a later date.

IPD sharing plan summary

Available on request