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Investigating the effects of nimodipine on spinal reflex measures in humans

Submission date
18/04/2024

Recruitment status
No longer recruiting

Registration date
24/04/2024

Overall study status
Completed

Last Edited
25/04/2024

Condition category
Signs and Symptoms

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

Type(s)
Public, Scientific

Contact name
Miss Eva Rudjord Therkildsen

ORCID ID
https://orcid.org/0000-0003-4797-1050

Contact details
Blegdamsvej 3B
Copenhagen
Denmark
2200
+4553551864
ertherkildsen@sund.ku.dk

Type(s)
Principal investigator

Contact name
Prof Jakob Lorentzen

ORCID ID
https://orcid.org/0000-0002-7634-0218

Contact details
Blegdamsvej 3B
Copenhagen
Denmark
2200
+45 31 52 11 31
jlorentzen@sund.ku.dk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
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 Copenaghen (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