Thermoregulatory responses of patients with EHS or MHS compared with healthy controls

Published: 15-02-2021
Last updated: 08-04-2024

To examine the thermophysiological responses to prolonged exercise in hot and humid environmental conditions in patients with a history of exertional heat stroke or malignant hyperthermia susceptibility and compare the thermophysiological responses...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON51224

Source
ToetsingOnline

Brief title
THREM study

Condition

- Other condition

Synonym
excessive hyperthermia, Heat stroke

Health condition

Thermoregulatoire aandoeningen (hitteberoerte en maligne hyperthermie)

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Exertional heatstroke, Malignant hyperthermia, Thermoregulatory resonses during exercise

Outcome measures

Primary outcome

The primary outcome of this study is the increase in core temperature (CBT)

during exercise at a fixed metabolic heat production.

Secondary outcome

Secondary outcomes relate to the thermoregulatory (i.e. skin temperature, heat

production, sweat rate, heat balance) and cardiovascular responses (i.e. heart

rate, blood pressure) to exercise in hot environmental conditions.

Study description

Background summary

Exercise is, due to the inefficient energy production, known to increase core body temperature (CBT), which could lead to substantial reductions in exercise performance and it increases the risk to develop heat-related illnesses such as heat exhaustion and heatstroke. Exertional heat stroke (EHS) is defined as a core temperature (>40.5°C) in combination with central nervous dysfunction resulting from exposure to environmental heat and strenuous physical exercise. EHS can be extremely dangerous, as it could lead to multiple organ failure, coma or even death. Previous literature suggested that some predisposing factors may put individuals at increased risk of EHS. However, the exact mechanism why some individuals suffer from events of EHS during a specific exercise and environment, while others do not, is not yet known. A related medical condition associated with dysregulation of the thermoregulatory system is malignant hyperthermia (MH). MH is a well described pharmacogenetic disorder with autosomal dominant inheritance. It clinically manifests as a

hypermetabolic crisis when an MH-susceptible (MHS) individual is exposed to volatile anesthetics or depolarizing muscle relaxants. Previous literature suggested that EHS may be related to MH, taking into account the overlap in symptomatology. However, it remains unclear whether patients susceptible to MH or EHS have an altered thermophysiological response to prolonged exercise challenging environmental conditions compared to healthy controls.

Study objective

To examine the thermophysiological responses to prolonged exercise in hot and humid environmental conditions in patients with a history of exertional heat stroke or malignant hyperthermia susceptibility and compare the thermophysiological responses with healthy age-matched controls.

Study design

Explorative intervention study.

Study burden and risks

Participants will visit the Radboudumc twice; medical screening and submaximal exercise test during visit 1 and providing a blood sample during visit 2. The burden of the exercise test is low, since all participants are accustomed to regular exercise training (endurance exercise *2x per week). For safety reasons, participants will be closely monitored during the exercise test. The test can be aborted when termination criteria (i.e. CBT *40°C) are met or if the participants decide to stop. Moreover, cooling interventions will be available when a participant develops symptoms of a heat-related illness. Furthermore, blood will be drawn from an antecubital vein, which may occasionally (<5%) result in a hematoma that will disappear usually within a week. Taken together, the burden and risks of the present study can be considered as negligible.

Contacts

Public
Radboud Universitair Medisch Centrum

Philips van Leijdenlaan 15
Nijmegen 6525EX
NL
Scientific
Radboud Universitair Medisch Centrum

Philips van Leijdenlaan 15
Nijmegen 6525EX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Between 18 and 60 years of age
- Willingness to provide written consent after proper information about the study objectives and procedures
- Physically active lifestyle (endurance exercise, *2 times a week)

Furthermore, we will apply specific inclusion criteria for the EHS and MHS group.
- EHS group: a history of an EHS in the past 10 years that has resulted in physical complaints for at least 6 months.
- MH group: a history of RYR1-related MH or MH susceptibility (MHS) according to the guidelines of the European Malignant Hyperthermia Group (EMHG), which states that an individual is MHS when an individual have a diagnostically confirmed RYR1 variant or a positive in vitro contracture test. Only one member per family will be included in order to ensure that we include a representative sample of the MHS population.
- Control group: healthy age and sex matched peers.

Exclusion criteria

A potential participant who meets any of the following criteria will be excluded from participation in this study:
- Exclusion criteria associated with the use of the telemetric temperature capsule: I) a bodyweight <36.5 kg, II) an implanted electro-medical device,

III) a history of obstructive/inflammatory bowel disease or surgery, IV) or a scheduled MRI scan within 5 days of the experiment.
- Medication use that alters thermoregulatory function (i.e. diuretics, laxatives and antihypertensives (disturbed fluid balance), anticholinergics and antiepileptics (reduced sweating), corticosteroids (impairs immune response and cytokine release), sympathomimetics (reduced vasomotor control), antipsychotics (disturbed thermoregulation in hypothalamus and reduced sweating)).

Additional exclusion criteria for the control group:
- A (family) history of EHS or MH
- A (family) history of suspected MH reactions
- A family history of RYR1 related myopathies (e.g. central core disease, King-Denborough Syndrome or multi mini core disease).
- A family history of an unexplained peri-operative dead

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-05-2021
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO

Date:	15-02-2021

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL76228.091.20

Study results

Date completed:	13-05-2022
Actual enrolment:	45