

The effects of concentration/meditation on the innate immune response during human endotoxemia

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Primary objective: The primary objective of the study is to determine the effect of concentration/meditation on the innate immune response induced by a lipopolysaccharide (LPS) challenge. Secondary Objective(s): There are two secondary objectives:1...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON36635

Source

ToetsingOnline

Brief title

LPS-concentration/meditation

Condition

- Autoimmune disorders
- Bacterial infectious disorders

Synonym

blood poisoning/sepsis

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Concentration, Endotoxemia, Inflammation, Meditation

Outcome measures

Primary outcome

The main study parameter is the concentration of circulating TNF- α following LPS administration.

Secondary outcome

Secondary study parameters include temperature, hemodynamic parameters (blood pressure and heart rate), illness score, catecholamines, heart rate variability, muscle sympathetic nerve activity, electroencephalography, other circulating cytokines (IL6, IL10 and IL1RA) and subclinical renal injury.

Study description

Background summary

The innate immune response is the first line of defense against invading pathogens. Ideally, this inflammatory response is tightly regulated leading to both adequate protection to invading pathogens as well as limitation of an exuberant or unwanted immune response such as seen in sepsis or auto-immune diseases. Certain individuals master a concentration/meditation technique involving a special breathing pattern which allows them to achieve remarkable feats, such as withstanding extreme coldness. This technique might influence the autonomic nervous system (ANS), since the ANS has a major influence on thermoregulation. This could represent a novel, non-pharmacological mechanism, to modulate the immune system since the ANS plays an important role in the regulation of the innate immune response. Activation of the sympathetic division of ANS dampens inflammation via β 2-adrenoceptors. The parasympathetic branch of the ANS modulates the inflammatory response as well, since it was discovered that electrical stimulation of the efferent vagus nerve in rats greatly inhibits the innate immune response. Modulation of ANS activity could therefore provide novel therapeutic options in limiting the inflammatory response. In the present study we wish to investigate the effect of concentration/meditation on the innate immune response in vivo. In addition we

wish to elucidate the mechanism via which this effect is mediated (e.g. the autonomic nervous system). We aim to use the so called human endotoxemia model. This model permits elucidation of key players in the immune response to a gram negative stimulus in vivo, therefore serving as a useful tool to investigate potential novel therapeutic strategies in a standardized setting. Since the concentration/meditation technique can be taught to other individuals, it could represent new treatment modalities for inflammatory conditions.

Study objective

Primary objective: The primary objective of the study is to determine the effect of concentration/meditation on the innate immune response induced by a lipopolysaccharide (LPS) challenge.

Secondary Objective(s): There are two secondary objectives:

1. To determine the effects of concentration/meditation on ANS activity. Electroencephalography (EEG), heart-rate variability (HRV), muscle sympathetic nerve activity and plasma concentrations of catecholamines will be measured for this purpose.
2. To determine if concentration/meditation can attenuate (subclinical) renal damage known to occur during human endotoxemia, markers of proximal and distal tubular damage will be measured at various time points.

Study design

Case-control study in a healthy male volunteer during experimental endotoxemia using historical controls.

Intervention

The day of the experiment, prehydration will be performed by infusion of 1.5 L 2.5% glucose/0.45% saline solution in 1 hour before LPS administration. LPS derived from E coli O:113 will be injected (2 ng/kg i.v., infusion rate; 1 minute).

Study burden and risks

A medical interview and physical examination are part of this study. On the day of the experiment, the volunteer will be monitored on the research unit of our intensive care and receive an arterial line to facilitate blood pressure monitoring, drug infusion during venous occlusion plethysmography and blood sampling. The arterial line will be placed under local anaesthesia using 2% lidocaine. Furthermore a venous cannula will be placed for the administration of saline and glucose. Muscle sympathetic nerve activity (MSNA) will be performed throughout the study using microneurography. A sterile microelectrode will be inserted manually through the skin in the underlying peroneal nerve below the fibular head. A second reference electrode will be placed

subcutaneously.

The administration of LPS induces flu-like symptoms for approximately 4 hrs. This model of systemic inflammation has been applied for many years in various research centres in the world. Endotoxin administration is considered safe and no long-term effects have been observed.

At the Radboud University Nijmegen Medical Centre, over 150 volunteers have received over 250 injections of lipopolysaccharide. Therefore, there is sufficient experience with this model at this centre.

In total, approximately 350 ml blood will be drawn during the experiment and urine will be collected.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

One male volunteer who masters the concentration/meditation technique.

Exclusion criteria

Use of any medication.

Smoking.

Bleeding disorder.

Previous spontaneous vagal collapse.

History, signs or symptoms of cardiovascular disease.

Cardiac conduction abnormalities on the ECG consisting of a 2nd degree atrioventricular block or a complex bundle branch block.

Hypertension (defined as RR systolic > 160 or RR diastolic > 90).

Hypotension (defined as RR systolic < 100 or RR diastolic < 50).

Renal impairment (defined as plasma creatinin >120 µmol/l).

Liver enzyme abnormalities or positive hepatitis serology.

Positive HIV serology or any other obvious disease associated with immune deficiency.

Febrile illness in the week before the LPS challenge.

Participation in another drug trial or donation of blood 3 months prior to the planned LPS challenge.

Study design

Design

Study type: Interventional

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Prevention

Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 09-03-2011

Enrollment: 1

Type: Actual

Ethics review

Approved WMO

Date: 15-07-2010

Application type: First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date: 03-02-2011

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
EudraCT	EUCTR2010-021457-39-NL
CCMO	NL32999.091.10
Other	volgt