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Pharmacological modulation of heterosynaptic LOng-TErm POtentiation in humans by LOrazepam and METHylphenidat

Submission date	Recruitment status	[ ] Prospectively registered
20/08/2007	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
24/09/2007	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
24/09/2007	Signs and Symptoms	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Rolf-Detlef Treede

Contact details
Institute of Physiology and Pathophysiology
The Johannes Gutenberg University of Mainz
Duesbergweg 6
Mainz
Germany
55128
treede@uni-mainz.de

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Tr 236/16-2/LTP-Methyl-Lora

Study information

Scientific Title

Acronym
LOTEPOLOMETH

Study objectives
Long-Term Potentiation (LTP) within the nociceptive system is one of the mechanisms underlying central sensitisation, which accounts for some hyperalgesic pain states in chronic pain patients. In the study we will use a human surrogate model of nociceptive LTP to study the involvement of the GABAergic and the catecholaminergic system in the induction of hyperalgesia following high-frequency electrical stimulation of nociceptive afferents in the skin.

We will study the contribution of GABAA-receptors (by lorazepam, a GABAA-receptor agonist) and receptors of catecholamines (by methylphenidat, a dopamine/noradrenaline re-uptake inhibitor) in plastic changes within the nociceptive system, which occur typically after a tissue injury, but in contrast to a real lesion we mimic an injury by high-frequency electrical stimulation of nociceptive afferents in the skin. This conditioning stimulation will lead to pain to light tactile stimuli (dynamic mechanical allodynia) and to an increase of pain to punctuate mechanical pain stimuli (static mechanical hyperalgesia). Both phenomena can typically been found in a subset of neuropathic pain patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The study was approved by the Local Ethics Committee (Ethikkommission der Landesärztekammer Rheinland-Pfalz) on 15 March 2003 (ref: 837.002.03[3664]) and was conducted in accordance with the declaration of Helsinki, the German Medicines Act (AMG), and the guidelines of the International Conference on Harmonisation (ICH) for Good Clinical Practice (GCP).

Study design
A double-blind, randomized, placebo-controlled, three-way cross-over study.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Quality of life

Participant information sheet

Health condition(s) or problem(s) studied
Hyperalgesic pain

Interventions
The effect of 40 mg methylphenidate and 2.5 mg lorazepam orally (p.o.) will be compared to placebo in a three-way cross-over design (placebo-methylphenidate-lorazepam). Sensory changes will be determined by Quantitative Sensory Testing (QST) using non-nociceptive and low-intensity painful mechanical and electrical stimuli.

The QST-protocol consists of mildly painful and non-painful mechanical and electrical stimuli, which were applied in runs alternating between two skin sites on the forearms (a test site and a control site). In addition, we will apply a moderate painful high-frequency electrical stimulation protocol to induce nociceptive LTP (only at the test site). All test stimuli will last between 0.5 - 2 seconds depending on the modality tested.

The QST will be carried out over 30 min before the application of the conditioning stimulus and over 90 min at the beginning and immediately after the stimulus.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Methylphenidate, Lorazepam

Primary outcome measure
The following outcomes will be assessed based on the sensory changes determined by QST during the intervention:
1. Spread of the area of dynamic allodynia and static hyperalgesia
2. Combined analgesic and anti-hyperalgesic effect to mechanical and electrical stimuli on the site of conditioning stimulation

Secondary outcome measures
The following outcomes will be assessed based on the sensory changes determined by QST during the intervention:
1. Anti-hyperalgesic effect to electrical and mechanical test stimuli
2. Analgesic effect to electrical and mechanical test stimuli
3. Anti-wind up pain, tested by mechanical pinprick stimuli

Overall study start date
01/10/2006

Completion date
01/10/2007

Eligibility

Key inclusion criteria

1. Healthy volunteers of full age
2. Subject familiarized with the experimental procedure prior to experimentation and had given written informed consent
3. At least a 50% increase of pain to pinprick stimuli and a 25% increase of pain to electrical stimuli following high-frequency electrical stimulation in a screening visit

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
18

Key exclusion criteria
1. Skin lesions at the test and/or control site
2. Use of any medication within one day prior to study onset except contraceptives
3. Known hypersensitivity to histamine or methylphenidate and lorazepam and their derivates
4. Any history of allergy or drug hypersensitivity
5. Chronic use of analgesics or Central Nervous System (CNS) active drugs
6. Pregnancy or nursing
7. Any acute or chronic disease

Date of first enrolment
01/10/2006

Date of final enrolment
01/10/2007

Locations

Countries of recruitment
Germany

Study participating centre
Institute of Physiology and Pathophysiology
Mainz
Germany
55128

Sponsor information

Organisation
Individual sponsor (Germany)

Sponsor details
c/o Prof Rolf-Detlef Treede
Institute of Physiology and Pathophysiology
The Johannes Gutenberg University of Mainz
Duesbergweg 6
Mainz
Germany
55128
+49 (0)61313925715
treede@uni-mainz.de

Sponsor type
Other

Website
http://www.uni-mainz.de/eng/index.php

Funder(s)

Funder type
Other

Funder Name
German Research Foundation (Deutsche Forschungsgemeinschaft) (Grant ref: Tr236/16-2)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration