Control of heart rhythm by the brain: the impact of stress-induced reductions in amygdala and hippocampus GABA activity on cardiac electrophysiology (BrainBeatS)

Published: 25-01-2018
Last updated: 12-04-2024

1. Induce acute stress in healthy volunteers and study whether changes occur in some of the main ECG indicators of ANS control of cardiac electrophysiology.2. Visualize and quantify the neurochemical effects in the brain (including amygdala and...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON46454

Source
ToetsingOnline

Brief title
BrainBeatS

Condition

- Other condition
- Heart failures

Synonym
sudden cardiac death (SCD)

Health condition

stress and the brain

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Hartstichting

Intervention

Keyword: brain, GABA, heart, stress

Outcome measures

Primary outcome

o ECG markers of ANS control: heart rate (HR), heart rate variability (HRV)

o Concentrations of GABA and glutamate in amygdala and hippocampus

Secondary outcome

o Stress markers: The State-Trait Anxiety Inventory (STAI), Perceived Stress

Reactivity Scale (PRSR), Barratt Impulsiveness Scale (BIS), life event

questionnaire, saliva biomarkers of stress (cortisol) and catecholamines

(alpha-amylase10), blood pressure

o Amygdala and hippocampus connectivity after the SECPT and control condition

(fMRI).

Study description

Background summary

Stress can strongly affect health and, among others, has an impact on cardiovascular outcomes, including sudden cardiac death (SCD) (Lampert, 2016). SCD is mostly due to cardiac arrhythmia (ventricular fibrillation, VF). Similar to other heart diseases with a sudden onset (e.g., acute myocardial infarction, AMI), SCD may be triggered by a disrupted autonomic nervous system (ANS) control of the heart. Indeed, SCD has been associated with stress, including

increased cortisol levels. However, the mechanisms whereby a disruption of ANS control affects cardiac physiology is incompletely understood. This project aims to fill this gap by studying whether acute changes in gamma-aminobutyric acid (GABA) and glutamate levels in the brain induced by acute stress impacts on electrocardiogram (ECG) indicators of ANS control of cardiac physiology.
We focus on the GABAergic system and amygdala and hippocampus, as GABA is the main inhibitory neurotransmitter in the brain (its concentration in the brain is 200-1000 times greater than that of the monoamines or acetylcholine). Neurosteroids, such as cortisol, that potentiate the inhibitory actions of GABA by, among others, modulation of the GABA-A receptor produce anxiolytic effects by the action on the amygdala, and GABA antagonists induce anxiogenic effects (Davis & Whalen, 2001). Furthermore, Takotsubo cardiomyopathy has been reported during withdrawal from multiple GABA agonists (e.g., benzodiazepine), which is thought to follow a sudden decrease in GABA signaling (Penget et al., 2016). We will also study glutamate, the main (mostly stimulatory) neurotransmitter in the brain.

Study objective

1. Induce acute stress in healthy volunteers and study whether changes occur in some of the main ECG indicators of ANS control of cardiac electrophysiology.
2. Visualize and quantify the neurochemical effects in the brain (including amygdala and hippocampus GABA and glutamate levels) induced by acute stress.
3. Associate ANS and GABA/glutamate levels with stress markers and brain activity.

Study design

Within-subject design

Intervention

The socially evaluated cold-pressor test (SECPT)

Study burden and risks

Risk assessment:
- MRI is a non-invasive imaging modality. All volunteers will receive extensive information about the MRI procedures beforehand. Volunteers suffering from claustrophobia will be excluded.
- SECPT is an evaluated stress test without any risks for participants.

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

- Male
- Age 20-35 years
- no heart and vascular disease history
- no psychiatric disorder history

Exclusion criteria

- General contraindications for MRI (such as claustrophobia)
- heart and vascular disease history
- psychiatric disorder history

Study design

Design

Study type:	Interventional
Intervention model:	Other
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	25
Type:	Anticipated

Ethics review

Approved WMO

Date:	25-01-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL64376.018.17