The three hit hypothesis of psychopathology revisited in a human model exposed to transient endogenous glucocorticoids excess: patients treated for Cushing's syndrome

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To understand, from the perspective of the 3-hit hypothesis of psychopathology, individual differences in the neuropsychiatric outcome of previous glucocorticoid (GC) excess in treated Cushing patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Observational non invasive

Summary

ID

NL-OMON35930

Source
ToetsingOnline

Brief title
The three hit hypothesis of psychopathology in Cushing's syndrome

Condition

- Hypothalamus and pituitary gland disorders

Synonym
Cushing's syndrome, Hypercortisolism

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Clinical severity, Cushing's syndrome, Early-lIfe stress, Genetic variation

Outcome measures

Primary outcome

1. What are the persistent effects of a transient excess of cortisol in treated

Cushing patients?

2. Can we validate the three hit hypothesis of psychopathology in treated

Cushing patients in order to distinguish the vulnerable from the resilient

individuals for persistent psychopathology in the aftermath of CS?

Secondary outcome

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Study description

Background summary

A fundamental question in the neurobiology of mental disorders is why depression and psychosis precipitate in some vulnerable individuals, while others remain healthy and resilient during stress exposure. Genetic variation in interaction with exposure to emotional neglect in early-life may program vulnerability to stress in later life as a basis for individual differences in psychopathology. We recently validated this i.e. 3-hit hypothesis in an animal model.

Study objective

To understand, from the perspective of the 3-hit hypothesis of psychopathology,

individual differences in the neuropsychiatric outcome of previous glucocorticoid (GC) excess in treated Cushing patients.

Study design

Subproject 1: extending the phenotyping of treated Cushing patients in more detail: Psychopathology and personality traits will be assessed. The current status of attention processing and vigilance of the patients will be measured by acoustic startle eye-blink response (together with its modulation by prepulse). Finally, with a facial recognition task we will investigate memory processes under mild social stress (Trier Social Stress Test).

Subproject 2: validation of the three hit hypothesis of psychopathology in the human, in treated Cushing patients: We will additionally perform this *3-hit analysis* on previously published measures of personality and cognitive performance of the same patients.

Study burden and risks

The patients are asked to come to the LUMC, where they are asked to:

- provide saliva
- complete a series of questionnaires
- undergo a structured interview
- do a computer task which is interrupted by a social stress task. During the computer task, the patient gets small electrodes under the eyes to measure the eye-blink.

Overall, patients spent approximately 3 hours, and there are no risks associated with this study.

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

- men and women between 18 and 70 years of age
- patients treated for Cushing's syndrome
- adequately substituted
- patients should be prepared and well informed about the study
- patients should sign the informed consent

Exclusion criteria

- difficulty to understand the Dutch language
- insufficient clinical data
- head trauma or CVA
- dementia
- alcohol or drugs abuse

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2011
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	23-06-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL36306.058.11