Neural correlates of chronic fatigue syndrome

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Primary objectives: - Identify neural correlates and behavioural measures that underlie cognitive processes that perpetuate CFS symptoms- Identify neural mechanisms of change that mediate successful CBTWe will focus our investigation on three...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Somatic symptom and related disorders
Study type	Observational invasive

Summary

ID

NL-OMON38461

Source
ToetsingOnline

Brief title
Neural correlates of chronic fatigue syndrome

Condition

- Somatic symptom and related disorders

Synonym
Chronic fatigue

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Muller Foundations

Intervention

Keyword: Chonic fatigue syndrome, cognitive behavioural therapy, fMRI

Outcome measures

Primary outcome

Main study parameters/endpoints:

- Blood Oxygenation Level Dependent (BOLD) signal as measured with functional Magnetic Resonance Imaging (fMRI)

- Cerebral tissue properties as measured with Magnetic Resonance Imaging (MRI) and Diffusion Tensor Imaging (DTI).

- GABA and NAA concentration as determined by MR-spectroscopy

- Behavioural performance on computerized tasks

- Subjective measurements, e.g. self-report questionnaires, visual analogue scales

- (Psycho) Physiological recordings e.g. surface electromyography (EMG) recordings, hart rate and respiration.

- Cortisol and cytokine protein concentrations from hair, saliva and blood samples

- Markers of sleep as measured with an ambulant electroencephalogram recording system

Secondary outcome

nvt

Study description

Background summary

Chronic fatigue syndrome (CFS) is characterized by profound disabling fatigue with an unknown aetiology. CFS is currently treated with Cognitive behavioural therapy (CBT), which has proven to be a successful therapy leading to a reduction in fatigue and disability. Consistent with cognitive behavioural models of CFS, recent clinical research has shown that mainly cognitive factors mediate successful therapy outcome. Accordingly, with support from neuroimaging studies, it has been suggested that central (cognitive) mechanisms play a role in CFS and its treatment. This project aims at identifying the neural correlates of central mechanisms that perpetuate CFS symptoms and underlie the mechanisms of change of CBT. Our hypotheses are derived from a neurobiological hierarchical Bayesian model of medically unexplained symptoms (Edwards et al., 2012) that emphasizes the influence of dysfunctional beliefs on perception. According t this model, somatoform symptoms arise from an inference failure between prior beliefs and sensory evidence. Thus, it is hypothesized that fatigue-related beliefs may bias perception towards experiencing fatigue. This project aims at investigating neural correlates associated with inference processes that are thought to underlie CFS symptoms. In addition, we will assess how these mechanisms change during cognitive behavioural therapy.

Study objective

Primary objectives:
- Identify neural correlates and behavioural measures that underlie cognitive processes that perpetuate CFS symptoms
- Identify neural mechanisms of change that mediate successful CBT

We will focus our investigation on three hypotheses: We will assess the hypothesis that, compared to healthy controls

1> CFS patients show a general tendency to base perceptual decisions more on prior expectations than on sensory inputs by investigating the influence of expectancy-cues in a moving-dot paradigm. Identification of such a bias in CFS patients within the visual domain would indicate a fundamental vulnerability that may predispose subjects to develop medically unexplained symptoms.

2> CFS patients have a perceptual bias about how errors in physical performance are interpreted, such that an error due to too little physical effort is attributed or processed differently than an error due to too much physical effort. This will be tested by investigating feedback processing and associated neural mechanisms in a force-estimation task. The finding that CFS patients have biased feedback processing in a physical performance task provides an explanation for the systematically found underperformance of CFS patients in physical exercise tests.

3> CFS patients have a higher tendency to infer contingencies between cues and outcomes that are inconsistent with sensory evidence, by investigating adaptive and aberrant salience and associated neural mechanisms in the salience attribution task. This learning process is proposed to contribute to the development and retention of dysfunctional beliefs which is proposed to play an important role in the maintenance and aggregation of symptoms.

Secondary objectives:
- Identify biomarkers (i.e. stress hormones, cytokines and sleep) as correlates of changes in symptoms after CBT

Study design

Phase 1, Pilot: Observational behavioural study in which untreated CFS and healthy controls will be tested once on computerized behavioural tasks.

Phase 2, RCT: Randomized controlled trial (RCT) in which CFS patients receiving CBT will be compared with CFS patients on a waiting list and all patients will be compared with healthy controls.

Study burden and risks

There is no risk associated with this study. The time that subjects need to invest in this study encompasses one (pilot) or two (RCT) visits to the Donders Centre for Cognitive neuro-imaging. These visits wall take about 3* hours during which subjects perform two tasks in the fMRI scanner and one computerized behavioural task in a quit testing room. Subjects will have to lie in an MRI scanner for ~2 hours of which in total 60 minutes includes active involvement in computerized tasks. Patients in the waiting list condition will perform one additional baseline assessment (standard protocol for all referred patients before diagnosis and after treatment) after the second test session and prior to the start of their treatment. Additional measurements include saliva sampling, blood sampling and hair sampling.

Patients will receive care as usual provided by the expert centre for chronic fatigue. Patients in the waiting list condition will not wait longer than usual before they start with CBT, as the average waiting period for starting treatment is at least 6 months. The benefit of participating in the study is that patients will have a 66 percent chance that they can start directly with CBT instead of waiting for 6 months. Both patients and healthy controls will receive a small financial compensation for their time investment according to the Donders Institute regulations on participant compensation.

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

All subjects:
• >= 18 years <= 65 years;
• Women;
• Able to speak read and write Dutch;
• Predominantly right handedness;
• Give written informed consent;;Patients:
• Meet the 1994 US centre for Disease Control and Prevention criteria for Chronic Fatigue Syndrome (revised 2003)
• Severely fatigued, i.e. scoring >= 40 on the subscale fatigue severity of the Checklist Individual Strength (CIS);
• Severely disabled; i.e scoring >= 700 in the Sickness Impact Profile r_08 (SIPr08) total score; ;Healthy control:

• Scoring <= 35 on the subscale fatigue severity of the Checklist Individual Strength (CIS);
• Scoring < 700 in the Sickness Impact Profile r_08 (SIPr08) total score;

Exclusion criteria

• Infection or inflammation at the day of testing (Body temperature >= 38°C);
• Any injury to the right hand that confounds hand grip performance;
• A maximal voluntary contraction (MVC) that exceeds the maximal dispersion of the hand grip device (>400 Newton)
• (History of) long term use of anti-depressants, anti-anxiety medications, beta-blockers benzodiazepines, psycho-stimulants or sleep medication;
• Current major depressive or bipolar disorder
• (History of) Schizophrenia or delusional disorder.
• (History of) Anorexia nervosa or bulimia nervosa
• (History of) alcohol or substance abuse
• Severe obesity (BMI >= 40)
• Abnormal hearing or (uncorrected) vision;;MRI Contraindications:
• Irremovable metal objects in or around the body (e.g. braces, pacemaker, metal fragments, hearing devices);
• Claustrophobia;
• (History of) Epilepsy;
• Possible pregnancy or breastfeeding;

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-01-2014
Enrollment:	160
Type:	Actual

Ethics review

Approved WMO Date:	17-04-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-09-2015
Application type:	Amendment
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	NL43606.091.13