The effect of modafinil on fatigue, cognition and functional connectivity in low-grade glioma patients: a double-blind randomized trial.

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(1) investigating the influence of modafinil on fatigue, cognitive functioning, and quality of life of LGG patients, (2) assessing the correlation between (changes in) fatigue, cognition, and quality of life on the one hand, and functional…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON31528

Source
ToetsingOnline

Brief title
Modafinil in LGG patients

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain tumor, fatigue

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Fonds NutsOhra

Intervention

Keyword: Cognition, Fatigue, Functional connectivity, Glioma

Outcome measures

Primary outcome

The CIS will be used as main study parameter, as a measure of fatigue. Quality of Life will be assessed by means of the SF-36, BCM20, and MOS. The CES-D will be administered to investigate levels of depression. A neuropsychological test battery assessing a range of cognitive functions will be administered. MEG recordings will take place during resting state, which means no-task and eyes-closed; analyses will be done with synchronization likelihood. Assessment of all parameters will take place at baseline (pretreatment; t0), t1 (immediately after six weeks of first treatment with placebo or modafinil) and t2 (immediately after six weeks of second treatment with placebo or modafinil).

Secondary outcome

n.a.

Study description

Background summary

Modafinil has been shown to reduce fatigue and possibly cognitive deficits and mood in diverse patient groups, hereby increasing patients* quality of life. Most low-grade glioma patients suffer from fatigue. However, the effects of modafinil have never been investigated in a homogeneous group of low-grade glioma (LGG) patients. We have previously shown that cognitive functioning is correlated with synchronization of brain activity between different areas, a concept known as functional connectivity. Also, cognitive dysfunction in glioma patients was shown to correlate with functional connectivity patterns. It

remains to be determined whether fatigue also has a neurophysiological correlate in the brain, and whether a modafinil-induced reduction in fatigue and cognitive disturbances is reflected by changes in functional connectivity patterns. Understanding the neurophysiological correlates of fatigue will facilitate the development of rational treatment of this symptom in glioma patients.

Study objective

(1) investigating the influence of modafinil on fatigue, cognitive functioning, and quality of life of LGG patients, (2) assessing the correlation between (changes in) fatigue, cognition, and quality of life on the one hand, and functional connectivity in the brain on the other.

Study design

Double-blind placebo-controlled intervention study.

Intervention

Patients will randomly be divided into two groups. These groups will first receive six weeks of treatment (with either placebo or modafinil), followed by a wash-out period of one week. Hereafter, another treatment period of six weeks will take place, in which patient groups will receive placebo or modafinil (opposite of first treatment). Treatment will begin with 100 mg modafinil, or matching placebo, upon waking and at lunch (200 mg/day). After one week, the dose will be doubled (400 mg/day). If patients experience adverse events at the higher dose, they will be allowed to decrease the medication to the previous dose. Patients will continue treatment at either 200 mg/day or 400 mg/day until the third visit, six weeks after start of the treatment.

Study burden and risks

The burden of participation for patients consists of (1) a number of visits to the outpatients* clinic (at the three research moments), (2) administration of a neuropsychological test battery at the three research moments, (3) examination through magnetoencephalography (MEG) at the three research moments, and (4) use of modafinil and placebo for twelve weeks in total. The neuropsychological assessment and MEG measurements are non invasive and do not involve any risk. Minimal side effects of modafinil use have been reported. However, we believe that the possible decrease of fatigue symptoms and thereby enhancement in quality of life of patients is of great importance for their well-being, and feel that the burden and risk of participation are proportionate to the expected gains of 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

(1) Reported severe fatigue (score > 35) on the Checklist Individual Strength (CIS), (2) histologically proven LGG without signs of tumor recurrence in the last year, and (3) written informed consent.

Exclusion criteria

(1) anti-tumor treatment other than antiepileptic drugs (e.g. chemotherapy, radiotherapy, corticosteroids), (2) psychiatric disease or symptoms, (3) insufficient mastery of the English or Dutch language, (4) inability to communicate adequately.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-04-2009
Enrollment:	64
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Modafinil
Generic name:	Modiodal
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	24-09-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-01-2009
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
EudraCT	EUCTR2007-003102-10-NL
CCMO	NL18598.029.08