Depression in Multiple Sclerosis: The effectiveness of web-based self-help treatment

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The goal of this research project is to evaluate effectiveness of a cognitive behavioural therapy self-help intervention offered through the Internet in multiple sclerosis (MS) patients with a co-morbid depressive symptoms. With the online guided...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Central nervous system infections and inflammations
Study type	Interventional

Summary

ID

NL-OMON47566

Source
ToetsingOnline

Brief title
Web-based therapy for MS patients with depressive symptoms

Condition

- Central nervous system infections and inflammations
- Mood disorders and disturbances NEC

Synonym
Depressive Disorder, Multiple Sclerosis (MS)

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Stichting MS Research

Intervention

Keyword: Depression, Internet, Multiple Sclerosis, Problem Solving Treatment

Outcome measures

Primary outcome

Effect measurements will be taken at 0 weeks (first measurement) and upon conclusion of the treatment at five weeks, 4 months, 10 moths follow-up (post-tests). All measurement scales have shown to be reliable, valid and responsive, and have been widely used as an outcome measure in MS research and/or research on psychiatric conditions. Participants who score above the cut-off score of 20 on the BDI are invited for a structured clinical interview for depression and anxiety disorders (the World Health Organization's Composite International Diagnostic Interview; WHO CIDI, 1990). The CIDI interview is conducted by telephone, as well as the Percieved Need of Care Questionnaire (PNCQ) and the Expanded Disability Status Scale (EDSS). The PNCQ assesses the participants' perceptions of their needs for mental health care and the meeting of those needs.

Interview (post-test, only for respondents participating in the MRI-study): Depression section of the structured clinical interview for presence of depression disorder and suicidal ideation (World Health Organiszation (WHO) version 2.1). The CIDI establishes diagnoses according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) (28). The CIDI interview is conducted by telephone

Primary outcome measure is the Beck Depression Inventory (BDI-II). The BDI is a

self-report instrument for assessing the existence and severity of depressive symptoms (Beck et al. 1961). Each of the 21 items match a symptom of depression according to the DSM-IV (DSM-IV, 1994). The total score is calculated by adding all the items and lies in between 0 and 63. The sum of the scores indicates the severity of the depression. Scores of 0 to 13 represent minimal depressive symptoms, scores from 14 to 19 indicate mild depression, scores from 20 to 28 moderate depression and scores of 29 to 63 indicate severe depression.

Secondary outcome

Secondary outcomes include other measures of depression, problem solving skills, quality of life, well-being, disability level, social support, mastery, cognitive functioning, fatigue, anxiety and satisfaction.

For comparison with the data of the Netherlands Study of Depression and Anxiety (NESDA) we decided to use another instrument to assess depressive symptoms. The Inventory of Depressive Symptomatology (IDS) consists of 28 questions, to assess the severity of depressive symptoms (Rush et al. 1996). The IDS assess all the criterion symptom domains designated by the American Psychiatry Association Diagnostic and Statistical Manual of Mental Disorders - 4th edition (DSM-IV) (APA 1994) to diagnose a major depressive episode.

The Beck Anxiety Inventory (BAI) is a 21-question multiple-choice self-report inventory that is used for measuring the severity of an individual's anxiety (Beck et al. 1988). We also use the HADS (Zigmond & Snaith, 1983) to measure anxiety and depressive symptoms.

The EuroQol (Dolan, 1997) consists of the EQ-5D and EQ-VAS. The EQ-5D describes quality of life on 5 dimensions: mobility, self care, daily activities (work, study, etc.), pain or other symptoms and anxiety / depression. Each dimension consists of 3 possible answer categories: no problems, some problems, serious problems. The EQ-VAS is a scale from 0 to 100 on which the patient indicates how well they perceive their current health situation, where 0 is the worst possible health state and 100 the best imaginable health state.
The MSIS-29 (Hobert et al, 2001) is used to measure the impact of MS en de WHO-5 (Bech, 2004) for measuring well-being.

The Fatigue Severity Scale (FSS) (Krupp et al. 1989) is a 9-item scale, used to assess the severity of fatigue. The Multiple Sclerosis neuropsychological questionnaire (MSNQ) is a self-report screening that is used to measure of neuropsychological functioning in MS (Benedict et al. 2003). Three subscales of the Social Problem Solving Inventory - Revised (SPSI-R) are used to determine individual problem-solving skills (SPSI-R, D*Zurilla et al. 2002). Mastery is measured with the Mastery Scale (Pearlin et al. 1978). The Social Support Inventory (Stansfeld and Marmot, 1992) contains questions on details about social support from the four most intimate persons. Finally, the Client Satisfaction Questionnaire (CSQ-8) measures patient satisfaction with the intervention (de Brey, 1983).

Neuropsychological examination: an adapted version of the Brief Repeatable Battery of Neuropsychological Tests (BRB-N) will be performed in order to

accurately measure cognitive function. Neuroimaging: the main MRI read-out parameters are: whole-brain resting state functional connectivity and activation patterns of the amygdala during an emotional memory task. Additionally, conventional imaging metrics will be obtained, such as total brain volume, lesion volume, the number of cortical lesions and white matter integrity. In order to obtain these measures, the following MRI sequences will be scanned on a 3T MRI scanner (total scanning time is approximately 60 minutes):

* T1 weighted: measurement of *black-hole* volume (neuronal loss)

* T2/PD weighted: measurement of white matter lesion volume

* MPRAGE: volumetric brain measurements (white, grey and total brain volume) and registration for fMRI measurements.

* Resting state fMRI: measurement for functional connectivity of the whole brain and regions of interest (e.g., amygdala)

* Task-specific fMRI: during an emotional memory task brain activation will be measured (i.e., to investigate changes in amygdala activation patterns)

* Diffusion tensor imaging: integrity of white matter fibre bundles

* Double inversion recovery: number of (sub)cortical grey matter lesions

Study description

Background summary

Depressive symptoms are prevalent among persons with Multiple Sclerosis. Lifetime prevalence-rates of depression in MS ranges from 28-51%, compared to 10-15 % in the general population. However, depression is often not recognized in MS, patients do not seek treatment for depression and adequate treatment

tends to be lacking. Depression is related to poorer quality of life, disrupts social support and has been associated with fatigue, a decrease in working hours and cognitive impairment in MS-patients.
Effectiveness studies have shown that MS patients are receptive to treatment for their depressive episodes. Recently web-based self-help treatment has been demonstrated as an effective intervention for reducing depressive symptoms in patients with a depressive disorder. We expect it to be a promising approach to the treatment of co-morbid depression in MS patients, because it is easy accessible and can overcome disease-related barriers to participate in face-to-face counselling.
A pilot study has shown promising results (NL25173.029.08, 2008/92). The preliminary pilot findings presume that the web-based intervention is a feasible and effective treatment for depressive symptoms in MS. These findings strongly encourage us to proceed with this intervention, and to examine the effectiveness of this web-based self-help course for the treatment of depressive symptoms in MS in a randomized clinical trial. To the best of our knowledge, this will be the first randomized controlled study to evaluate effectiveness of a web-based self-help treatment in MS.

Study objective

The goal of this research project is to evaluate effectiveness of a cognitive behavioural therapy self-help intervention offered through the Internet in multiple sclerosis (MS) patients with a co-morbid depressive symptoms. With the online guided self-help Cognitive behaviour therapy (CBT) intervention we want to improve the level of care for people with MS and co-morbid depression. By recruiting and offering treatment through the Internet we can reach a group of underserved patients who normally do not seek or receive treatment for distress.

The aims of this study are twofold: 1) examine the effectiveness of the web-based CBT self-help intervention for MS-patients with depressive symptoms, and 2) compare characteristics of symptoms of depression and anxiety, quality of life, social support, perceived need of care and mastery in MS patients with co-morbid depression versus a cohort of patients with current depression.

Using the results of the RCT, we will address the following:
1. Is the web-based self-help intervention (cognitive behaviour therapy based on the principles of problem solving therapy) more effective in reducing depressive symptoms in MS patients than care as usual?
2. What are the effects of the web-based intervention at issue on anxiety, social support, cognitive functioning, quality of life, well-being, disability level and fatigue in MS patients with depressive symptoms?
3. Which predictors of a favourable outcome of the web-based intervention on depressive symptoms can be identified?

By comparing the RCT data with a large-scale available depression cohort from

the Netherlands Depression and Anxiety Study (NESDA):
4. Is there a difference in presentation of depressive symptoms in people with MS, compared to persons with a current depressive disorder (and no MS) and chronically ill with a co-morbid depressive disorder?

Neurobiological mechanisms underlying the positive effects of web-based self-help therapy
5) Does web-based self-help therapy to relieve depressive symptoms in MS patients alter resting state functional brain networks, as measured with functional magnetic resonance imaging (fMRI)?

6) What is the effect of web-based self-help therapy in patients with MS on the functional connectivity between the amygdala (important brain structure involved in depression) and other brain regions?

7) Does web-based self-help therapy in people with MS affect brain activation patterns of the amygdala during an emotional memory task (task-specific fMRI)?

Study design

The study is designed as a randomized clinical trial with 1 intervention arm and a care as usual control group. 166 MS patients with moderate to severe depressive symptoms will be randomly assigned to a treatment group or a care-as-usual control group. The treatment group will follow the web-based self-help intervention of 5 weeks. Outcome is evaluated before and after the intervention, at 4 and 10 months follow-up (only the intervention group to investigate the effects at longer term).
In case not all required 30 of the 166 included respondents completed the baseline and posttest of the neuropsychological testing and MRI scanning section of the study, we will continue this part of the randomized controlled trial until we included 30 respondents who are willing to participate in the neuropsychological testing and MRI scanning at baseline and post-assessment. In that case, respondents can only participate in the study if they agree with MRI and neuropsychological testing. Follow-up assessments (4 and 10 months) will be cancelled. (protocol page 6, 19)

The present study has been developed in collaboration with the Netherlands Study of Depression and Anxiety (NESDA; www.nesda.nl). NESDA is an ongoing cohort study designed to investigate the course and consequences of depressive and anxiety disorders. A detailed description of the NESDA study design and sampling procedures can be found elsewhere (Penninx, B. W., et al. The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. Int J. Methods Psychiatr Res 17, 121-140, 2008).

This third aim, to investigate the effect of online intervention on advanced neuroimaging parameters (functional networks and brain activation patterns) and

cognitive function, will be investigated with our colleagues: Prof. dr. J. Geurts, Prof. dr. F. Barkhof, drs H. Hulst from the department of Neurosciences and Radiology.

Intervention

The online cognitive-behavioural self-help treatment examined in this study is based on what is known as *problem-solving therapy* (PST). The original PST-based intervention for depression is extensively described by Cuijpers, van Straten, Warmerdam (2007). With a number of modifications we adjusted the intervention for people with MS and co-morbid depression, conserving the intent of the PST-based intervention. Modifications concerned additional information about MS and its psychosocial consequences and text and examples applying to MS patients. The intervention is called *minderzorgen*: (website: www.minderzorgen.nu)

The web-based intervention is a self-help intervention of five modules with text, exercises, and figures. The participants access the intervention from their personal computers via the Internet. The recommended time for completion of the course is five weeks, one session per week. Participants are asked to work on their assignments for at least 2 hours per week. In that period, respondents describe what they think is important in their lives, make a list of their problems and concerns, and divide these into three categories: unimportant problems (problems which are not related to what is important in their life), important and solvable (these are solved through a six-step procedure of problem-solving), and important but unsolvable (such as loosing someone through death; for each of these problems the respondent makes a plan how to cope with this). The six-step problem-solving method is the most important step of the intervention containing the following steps: (1) write a clear definition of the problem, (2) generate multiple solutions to the problem, (3) select the best solution, (4) work out a systematic plan for this solution, (5) carry out the solution, and (6) evaluate as to whether the solution has resolved the problem. Support during the intervention consists of communication through brief, weekly e-mails sent through the website, and will be provided by supervised clinical psychology Master students. The e-mail correspondence is intended to facilitate the patient*s effective use of the self-help method, and is explicitly not intended to build up a patient * therapist relationship. During the intervention, patients will receive four supportive text-messages (sms) per week on their mobile phone to support them during the intervention and to enhance compliance rate. Patients could not react on the text-messages.

Care as usual consists of the care provided by the health care centre visited by the patient. We will not intervene in the given care, and the patient is free to accept any intervention (medication, psychological treatment) given in the time period of the study. The received mental health care will be registered. If proven successful, we will provide the care as usual control

group the intervention on voluntary basis after the study has been finalized.

Study burden and risks

The burden of participation will be 4 hours of extra work, next to the intervention (14 hours). These 4 hours consist of:
-screening questionnaire (5-10 minutes)
-interview by telephone (45 minutes)
-pre-test: several questionnaires (45 minutes)
-3 x post-test: several questionnaires (45 minutes) (in case we included 166 patients but continue the study to include all the 30 patients for the MRI part of the study, two post-test will be cancelled (2 x 45 minutes)
-MRI-measurement/neupsychological testing/post-CIDI interview will take 5 hours (extra: 2 x 2,5 hours).

Participation in this study is without any risks

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

MS patients (minimum age 18) can take part if they: 1) are diganosed with MS 3 months befor the screening and 2) are able to manage the Dutch language. Inclusion criteria for the intervention are: 1) a minimum score of 20 on the Beck Depression Inventory (BDI-II), and the intention and capability to invest 5 weeks of their time to follow a selfhelp intervention through the internet.

Exclusion criteria

No access to Internet or no email-address, no experience with Internet, no sufficient command of Dutch, unable to read, current use of antidepressants or other treatment of depression, current suicidal ideation.
Subjects with contra-indications for MRI scanning or from Belgium will be excluded for the MRI study (see Onderzoeksprotocol, appendix 6, checklist MRI).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-07-2011
Enrollment:	201
Type:	Actual

Ethics review

Approved WMO Date:	12-07-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-07-2019

Application type:	Amendment
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	NL35191.029.11