Clinical pilotstudy in the effect and feasibility of online cognitive training on cognitive functions in patients with Parkinson's disease, Multiple Sclerosis and depressive patients treated with electroconvulsive therapy

Published: 03-12-2015
Last updated: 19-04-2024

The objective of this pilotstudy is primarily to assess a cost-efficient, easy accessible training of cognitive functions on its feasibility and initial effect in patients with cognitive dysfunction in PD, MS of patients treated with ECT. Using this...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45237

Source
ToetsingOnline

Brief title
Online cognitive training in Parkinson's disease, MS and postECT

Condition

- Other condition
- Movement disorders (incl parkinsonism)
- Cognitive and attention disorders and disturbances

Synonym
Cognitive deficit, Thinking problems

Health condition

MS, depressieve ouderen behandeld met ECT

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cognition, online, rehabilitation, training

Outcome measures

Primary outcome

The primary studyparameters aim to measure the feasibility of the intervention and challenge the patients experience while using the intervention. This will be measured by a questionnaire consisting of four-point Likert scales, which assess the patients' opinion of the intervention on several aspects.

Secondary outcome

The secondary study parameters are first off the training effect of the intervention, which will be measured by the interaction effect between time of measurement (T0 versus T1, of T0 versus T2) and condition (experimental versus control). If possible, parallel tests will be used to correct for repeated neuropsychological testing. The objectively measured training effect will be assessed on the most affected cognitive domain, different per syndrome:

- PD: change in executive functions, measured by change in the Trail Making Task, Stroop Color Word Test and Letter Fluency.

- MS: change in episodic memory, measured by change in the Rey Auditory Verbal Learning Test and/or the Location Learning Test.

- postECT: change in executive function, as measured by change in the Trail Making Task, Stroop Color Word Test and Letter Fluency.

Second, the secondary studyparameters are change in subjective cognitive complaints as reported by the patient, measured by the Cognitive Failure Questionnaire (CFQ).

Study description

Background summary

In neurodegenerative disorders and psychiatric disorders, cognitive dysfunction is frequently reported. In Parkinson's disease (PD), Multiple Sclerosis (MS) and patients treated with electroconvulsive therapy after a severe or therapy resistant depression (postECT), executive dysfunction are prevalent (Bosboom, Stoffers & Wolters, 2004; Chiaravalloti & DeLuca, 2008; Rubin, Kinscherf, Figiel & Zorumski, 1993). However, cognitive dysfunction is heterogeneous, within these groups as well as between, and it is not limited to one cognitive domain. In PD and MS, problems in attention and episodic memory are also frequently described (Bosboom et al. , 2004; Chiaravalloti & DeLuca 2008; Rao, Leo, Bernardin & Unverzagt, 1991). These dysfunctions can appear already early in the disease (Achiron & Barak 2003; Muslimovi*, Post, Speelman & Schmand, 2005). The majority of PD patients - estimations are about 80% - develops PD dementia (Aarsland, Andersen, Larsen, Lolk & Kragh-Sørensen, 2003; Hely, Reid, Adena, Halliday & Morris, 2008). In MS, about half of the patients experiences problems in cognitive functions (Rao et al., 1991). ECT can recover patients with severe and/or therapy resistant depression. However, 30-50% of these patients develops severe cognitive dysfunction in the executive dysfunction as well as in attention and autobiographical memory (Rubin et al., 1993; Oudega et al. 2014). Recovery appears often within six months after ECT. However, performances remain below-average compared to normgroups and there are large individual differences (Verwijk et al., in prep.). The cognitive difficulties in MS and PD have a significant negative influence on the quality of life (Chiaravalloti & DeLuca 2008; Klepac, Trkulja, Relja & Babi*, 2008). Cognitive dysfunction in PD is associated with decreased independent daily functioning, hospitalization and the development and severity of neuropsychiatric symptoms (Fletcher, Leake, Marion, 2011). Furthermore, in the clinic cognitive

dysfunction has been reported to be one of the most dreadful side effects of ECT. However, effective treatment of the described cognitive dysfunction is still in its infancy, possibly due to heterogeneity in cognitive problems and the pathological mechanisms that underly these (Hoffmann, Tittgemeyer & Von Cramon, 2007; Guimarães & Sà, 2012; Gerrits et al., 2014; Robbins & Cools, 2014; Verwijk et al., in prep.). For example, pharmacological interventions using levodopa or cholinesteras-inhibitors are very limitedly effective (Svenningson, Westman, Ballard & Aarsland, 2012).

Cognitive training is based upon the principle that plasticity of the brain can facilitate function improvement by intensive training. In Alzheimer's disease, cognitive training has shown significant improvemend in cognitive functions (Olazaran et al., 2010) and in traumatic brain injury cognitive training is advised to treat cognitive dysfunction (Cicerone et al., 2011). Moreover, complex cognitive training has shown positive effects on cerebral bloodflow and functional and structural connectivity in healthy elderly (Chapman et al., 2015). A meta-analysis in Alzheimer's disease showed that restorative training methods (i.e. training specific functions) had larger effect sizes as compared to compensatory training methods (e.g. strategy training) (Sitzer, Twamley & Jeste, 2006). Furthermore, computerized training methods have shown larger, or at least comparable effect sizes as compared to traditional pen-and-paper methods in healthy elderly (Kueider, Parisi, Gross & Rebok, 2012). In MS and PD, there have been earlier studies in the effect of cognitive training on functioning. In MS, a memory training was shown to be specifically effective in patients with moderate cognitive dysfunctions (Chiaravalloti, DeLuca, Moore & Ricker 2005). In PD, a systematic review showed that various cognitive training methods (e.g. pen-and-paper, simple sudoku, computer training) had small to large effects on cognitive functioning (Hindle, Petrelli, Clare & Kalbe, 2013). However, earlier studies have been small, frequently without a controlled design (Hindle et al., 2013; Rösti-Otajärvi & Hämäläinen, 2011). Additionally, earlier cognitive training programs have frequently been executed in a health care organization, impairing patients to successfully attend all training sessions due to mobility impairments. Also, there are limited studies in the effects of cognitive training on improved functioning of daily living and neuropsychiatric symptoms like anxiety and depression. Given the fact that there is an absence in cognitive training studies in patients post-ECT, there is no knowledge about the ability of cognitive training to speed up the natural course.

Using this pilotstudy, we aim to study the feasibility of a randomized controlled trial using an online computerized intervention for training cognitive abilities in three patient groups. By using a double-blinded, controlled study design, we keep in mind limitations of earlier comparable studies. If this treatment proves to be feasible, and a rough estimated effect sized are positive, a larger randomized controlled trial can be executed to study the effectivity of this treatment. When effects are positive, an online cognitive training programme could prove to be a cost-efficient intervention that is accessible at home - something which is important for patients impaired

in mobility.

Study objective

The objective of this pilotstudy is primarily to assess a cost-efficient, easy accessible training of cognitive functions on its feasibility and initial effect in patients with cognitive dysfunction in PD, MS of patients treated with ECT. Using this pilotstudy, we aim to assess if a larger randomized controlled trial is feasible.
Primary objective: is BrainGymmer feasible and challenging in the previously mentioned syndromes?
Secondary objective: what is (an estimation of) the effect of BrainGymmer on the subjective cognitive functioning of the patient (as measured by both the patient and the caregiver) and the objective cognitive functioning of the patient (as measured by an extensive neuropsychological assessment) in PD, MS and patients treated with ECT?

Study design

This pilotstudy uses a double-blinded, randomized controlled design. N = 10 for each syndrome, and both intervention groups - total N = 60. Patients will be randomly and double-blind assigned to either the training intervention or the control condition. Both conditions will perform the training/activities 45-60 minutes a day, three times a week during eight weeks. Before the start, at the end of intervention and a month after the end of intervention, a neuropsychological assessment and questionnaires will be taken. After the end of the intervention, participants will be asked to review the intervention by filling in a questionnaire that uses four-point Likert scales.

Intervention

The intervention aims to train several cognitive abilities; especially the executive functions, attention, working memory and processing speed. The control condition consists of cognitive activities that do not intend to train cognitive functions, such as simple puzzles, domino and solitaire. An online training program, BrainGymmer (www.braingymmer.nl), is used to have patients perform the training sessions independently at home. The choice for this intervention is based on the fact that it is an online training method with challenging and (on the first sight) valid games, which is used in other (running) studies at the UvA and Leiden University (e.g. TAPASS - www.tapass.nl). The mental processes that are appealed to by the intervention are similar to processes that are trained in classic face-to-face training methods. Both the intervention protocol and the control condition will contain several games that have the participant train cognitive functions/perform cognitive activities for 45-60 minutes each session. The games are equipped with a so-called 'dynamic difficulty adjustment', which means that the

difficulty is adaptive to the participants' performance. Using this adjustment, the games adapt to the (baseline) cognitive abilities of each participants, and it challenges them to improve on each task. Furthermore, BrainGymmer is an interactive platform, wherein performances can be measured and compared to other participants in the study. During the intervention, the participants will be contacted every other week to evaluate the progression, to motivate them and to answer possible questions. Moreover, the patients' compliance will be recorded by BrainGymmer and will be sent every week to the researcher. The training games will be presented sequentially, until every game in the training protocol has been performed. In the PD-group, patients will be asked to perform the training/tasks an hour after taking their dopaminergic medication, to control for ON/OFF fluctuations. In this manner, patients will be trained in the ON-phase, to minimalize the effect of motor symptoms on performing the intervention.

Study burden and risks

In this study, the participant will be asked three times to visit the VUmc. At each visit, a neuropsychological assessment (± 60 minutes) and questionnaires (± 20 minutes) will be assessed. During the intervention patients will carry out an online training program or 'control' cognitive activities for 45-60 minutes, three times a week during eight weeks. The risk associated with this intervention is negligible, while the chances of improved cognitive functions are realistic on the basis of earlier research. The intervention is not specifically designed for one disease type; the intervention will be assessed in multiple disease wherein cognitive disorders are similar.

Contacts

Public
Vrije Universiteit Medisch Centrum

van der Boechorststraat 7
Amsterdam 1018BT
NL
Scientific
Vrije Universiteit Medisch Centrum

van der Boechorststraat 7
Amsterdam 1018BT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

General criteria:
- Patients have (access to) a computer with access to the Internet. Patients are capable of using a keyboard and computer mouse.
- Patients are willing to sign informed consent.
PD-specific criteria:
- Cognitive dysfunction is apparent on at least one out of three executive function tests (i.e. Stroop, Trail Making Task, Fluency), which is defined as follows: 30 <= T-score <= 43. T-scores are based on Dutch norm groups (e.g. Schmand, Houx & De Koning, 2012) that are distributed normally with M = 50 and SD = 10. In Dutch neuropsychology, these scores are used to correct testscores for age, sex and education effects.
- Patients are diagnosed with Parkinson's disease according to the United Kingdom Parkinson*s Disease Society Brain Bank criteria (Hughes, Daniel, Kilford & Lees, 1992).
- Patients are in Hoehn & Yahr stadium < 4, and are medically stable during a month prior to the intervention. The medication will be attempted to remain stable for the remainder of the intervention.
- Patients are 50 to 70 years old.
MS-specific criteria:
- At least one episodic memory task (i.e. Rey Auditory Verbal Learning Test, Location Learning Test) shows deficit, which lies at least 1 SD below the mean of healthy normpopulation (Schmand, Houx & De Koning, 2012).
- Patients have been diagnosed with MS for a period longer than three month prior to inclusion in this study according to the renewed McDonald criteria (Polman et al., 2011).
- Patients have been on stable medication for at least three months.
- Patients are 20 to 60 years old.
postECT-specific criteria:
- Unipolar depressive patients indicated for ECT, who experience cognitive complaints after treatment with ECT.
- Patients have undergone the full ECT-procedure.
- Phonemic fluency and/or autobiographical memory (measured by the Kopelman

Autobiographical Interview) show deficit: significant individual detoriation is present (> 1.0 SD detoriation), accounting for test- retesteffects.
- Patients are 18 to 100 years old.

Exclusion criteria

General criteria:
- Indications for presence of dementia.
- Presence of traumatic brain injury.
- A psychiatric disorder (in the postECT group: other than unipolar depression).
- No history or presence of drug or alcohol abuse.
- Inability to undergo a neuropsychological assessment (e.g. due to fast fatigue, seeing problems or language barrier).
PD-specific criteria:
- Psychotic symptoms, as screened by the Questionnaire for Psychotic Experiences (QPE). Benign hallucinations with insight are not contraindicated).
MS-specific criteria:
- Patients with MS can't have relapses or can't use corticosteroids 4 weeks prior to the start of the study.
postECT-specific criteria:
- Indications for presence of delirium.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-03-2016
Enrollment:	60

Type:	Actual

Ethics review

Approved WMO Date:	03-12-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-04-2017
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
ClinicalTrials.gov	NCT02525367
CCMO	NL54022.029.15