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Cognitive rehabilitation in multiple sclerosis

Submission date
14/10/2013

Recruitment status
No longer recruiting

Registration date
07/02/2014

Overall study status
Completed

Last Edited
25/01/2017

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Multiple sclerosis (MS) is a relatively common condition in the UK. Often symptoms begin in early adulthood and can lead to physical disability. Although less common, another symptom that may be associated with MS is difficulty with cognition (memory). It has become increasingly recognized that if present, these problems often relate to planning, information processing speed as well as memory. This study aims to understand why some individuals with MS experience memory problems, if certain forms of cognitive training can improve memory in these individuals and how if any this reflects changes in magnetic resonance imaging (MRI) brain scans.

Who can participate?
Patients diagnosed with MS. We know that some patients are aware of some memory problems and difficulty with planning as the condition progresses. We also know that some patients with MS have subtle memory problems that they may not be aware of and may not impact upon them. These are often only picked up on detailed examination. However, through studying patients with all levels of memory problems we may still learn much about cognitive problems in MS and for this reason all patients with MS may potentially be screened for memory problems and be considered for participation.

What does the study involve?
If you do decide to take part, we will first ask you sign the relevant consent forms. You will again have the opportunity to ask further questions. The initial step is to perform a brief cognitive assessment to see if you have any memory difficulties on formal testing. This will be carried out in the clinic and takes approximately 15 minutes. The tests will be of varying difficulty. There is no pass or fail on the tests, they are just to screen for the presence of any cognitive difficulties and establish a baseline before any cognitive rehabilitation takes place. It should be emphasised that all individuals will find certain aspects of the testing difficult at times.
At this stage, if there is insufficient evidence of significant memory problems you would not be asked to participate further in the study. If we detect cognitive difficulties above a certain level during these tests you would be invited to participate in the remainder of the study. At this point you will undergo a brief brain examination in order to ascertain if there are any physical disorders that might make participation in the study difficult. You will then be asked to complete a number of questionnaires relating to mood, fatigue and daily function. This will take about 15-20 minutes. If it is more convenient, the questionnaires may be completed when

attending for the first MRI scan. You will then be invited to have a MRI brain scan. This will be performed in the weeks following enrolment but before any training occurs. You will most likely have had a MRI scan previously as part of the diagnostic work up for MS. You will then be randomly allocated to one of two groups. One group (the active treatment group) will receive cognitive training on a home PC. This will involve three 45 minute sessions per week for 6 weeks. The other group will be the control group and while there will not be the home based cognitive training, you will receive a series of DVDs to watch for the same period for 6 weeks. This is to see if the cognitive training makes any difference to outcomes compared to the control group. Following completion of the 6-week study period, you will be asked to undergo MRI scans on two further occasions to examine if any change can be noticed on MRI. While attending for MRI you will be asked to undergo the same cognitive testing and complete the same questionnaires as before. The first of these MRI scans will be soon after completion of the 6-week study period and the second scan performed 3 months later. You will therefore have a total of three cognitive examinations as well as three MRI brain scans and you will be asked to complete the questionnaires on three separate occasions.

What are the possible benefits and risks of participating?
We cannot promise the study will improve your memory, but the information we get may help improve our understanding of some of the cognitive difficulties that individuals with MS may experience. It is hoped that this study will provide evidence for the effectiveness of the training to help improve memory in patients with MS who suffer from memory problems. The MRI scanning may help us better understand the areas involved in memory and devise techniques to earlier identify patients who may go on to develop memory difficulties. Participants will have to devote some of their personal time towards taking part in the study, in particular participants will have to devote a dedicated period to undertaking the training at home as well as undergoing three MRI scans. Taking part in this study will not affect the usual standard of care that you receive. All techniques that we use in the study are known to be non-invasive and safe. MRI has been used in clinical practice and research for over 20 years and is not associated with any long term side effects. MRI does involve a high strength magnetic field and therefore steps will be taken to ensure you have no metallic objects in your body as this could be dangerous. Very rarely during MRI scanning an incidental abnormality is detected. Under these circumstances an expert opinion may be sought with regards to the images. This is only done in the cases where it is believed there is a clear need and may require images and personal details being entered onto information systems owned and operated by Brighton and Sussex University Hospitals NHS Trust (BSUH). Following this, medically trained members of the research team will discuss the abnormality with you and you would be referred to the appropriate individual.

Where is the study run from?
The study is based in Sussex. At this stage we expect to recruit patients with MS who are attending Brighton and Sussex University Hospitals NHS Trust. The MRI scanning will be performed in the University of Sussex, Clinical Imaging Sciences Centre (Falmer campus).

When is the study starting and how long is it expected to run for?
November 2011 to September 2015

Who is funding the study?
Brighton and Sussex University Hospitals NHS Charitable Fund (UK)

Who is the main contact?
1. Dr Waqar Rashid, Chief Investigator
2. Dr Jamie Campbell, Clinical Research Fellow and Neurology Registrar at Brighton and Sussex University Hospitals NHS Trust

Contact information

Type(s)
Scientific

Contact name
Dr Waqar Rashid

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
139292

Study information

Scientific Title
A randomised study of cognitive rehabilitation in multiple sclerosis

Study objectives
This study has been designed to systematically investigate whether individuals with multiple sclerosis who exhibit cognitive dysfunction respond to a period of cognitive rehabilitation, both in terms of cognitive improvement and with respect to a variety of MRI measures. It is known that 40-70% of patients with MS have some degree of cognitive impairment. Participants and/or their relatives will frequently report cognitive difficulties but in some patients the deficits may be subclinical at an early stage.

Null Hypothesis
The null hypothesis is that
1. A period of cognitive rehabilitation does not influence cognitive performance or quality of life measures in individuals with MS.
2. There are no structural or functional MRI changes following active rehabilitation

The alternate hypothesis is that cognitive rehabilitation results in improved cognitive scores, quality of life outcome measures and leads to changes in structural and functional MRI parameters.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Northern Ireland REC, 27/11/2013, ref:13/NI/0182

Study design
Interventional single-centre randomised trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please contact Dr Jamie Campbell to request a patient information sheet

Health condition(s) or problem(s) studied
Neurology - multiple sclerosis and cognition

Interventions
Patients who have a previous diagnosis of multiple sclerosis and who are already attending a neurologist will be screened for eligibility during routine outpatient follow up appointments. Those reporting cognitive difficulties and are interested in the study will be invited to undergo brief cognitive assessment (BICAMS) which is estimated to take approximately 15-20 minutes. This will screen patients who have significant cognitive difficulties. It is anticipated that if eligible, they will undertake a series of additional questionnaires/assessments to address cognition, quality of life measures, disease management and mood. Each component is expected to take approximately 5 minutes with the initial BICAMS taking approximately 15 minutes. There is no time limit and participants can take a break at any stage.

Participants will be randomised to either undergo cognitive rehabilitation with Rehacom Software (x3 45 minute training sessions per week for 6 weeks) or be placed in the placebo arm to spend the same portion of time in the control condition (natural history DVDs). During this period they are expected to undertake three x 45 minute computer training sessions per week for the 6-week period. There will also be an MRI brain scan at baseline prior to undertaking the training. Following completion of the 6-week training period, both the full cognitive assessments and MRI scanning will be repeated immediately following the training period and again at approximately 3-6 months.

Full list of assessments

1. Disease management:
1.1. PAM-13 (Patient Activation Measure), a 13-item generic scale for chronic illness management, sometimes characterised as patient empowerment, validated in MS
1.2. Unidimensional Self-Efficacy scale for MS (USE-MS)
2. Mood: Hospital Anxiety and Depression Scale (HADS): a brief (14-item) measure of psychological distress, which provides separate scores for anxiety and depression. Due to its focus on thoughts and behaviours, instead of physical symptoms of anxiety and depression, it has been widely used in MS.
3. Self-report of cognition: MSNQ (Multiple Sclerosis Neuropsychological Questionnaire, patient completed). It is well established in the literature that patient self-report of cognition is confounded by depression
4. Fatigue: FSS (Fatigue Severity Scale)

Home PC required specs
1. PC with Pentium or compatible CPU with at least 2.5 GHz
2. At least 512 MB of RAM
3. 3D-graphic card compatible with DirectX 9.0 and at least 128 MB of RAM as well as a graphic chip by NVIDIA (GeForce FX5200 or better) or ATI (Radeon 9500 or better). The display driver must support Open-GL starting from version 1.4.
4. DVD drive, hard disk, mouse, keyboard

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Objective cognitive performance: BICAMS (Brief International Cognitive Assessment for MS), a 15-minute careening tool
2. Quality of life:
2.1. EQ-5D, a generic health-related quality of life scale
2.2. FAMS (Functional Assessment of MS), an MS-specific quality of life scale

Secondary outcome measures
MRI: The data will be acquired on the 1.5T Siemens machine. The following analyses will be completed:
1. Voxel-based morphometry
2. Tensor-based morphometry
3. Cortical thickness
4. Lesion load
5. Resting state analysis (DMN)
6. DTI analysis

Overall study start date
01/11/2013

Completion date
30/09/2015

Eligibility

Key inclusion criteria
1. Diagnosis of MS by consultant neurologist to best current criteria
2. Able and willing to give informed consent
3. Cognitive impairment defined by scoring below 5th percentile on one or more of Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) scales as identified at the clinic
4. Willing to commit to three 45-minute computer training sessions for six weeks
5. Home PC fulfilling experimental spec
6. Willing to attend total of 3 MRI scans at the University of Sussex MRI scanner
7. Age between 18 and 70

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
50

Key exclusion criteria
1. Significant change in medications in last 4 weeks
2. Relapse recovery within last 4 weeks
3. Sensorimotor dysfunction likely to interfere with PC interface
4. Significant psychiatric history/condition
5. Significant medical condition (other than MS), personal or social circumstances likely to influence cognition or study participation
6. Women who are pregnant

Date of first enrolment
01/11/2013

Date of final enrolment
30/09/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Sussex County Hospital
Brighton
United Kingdom
BN2 5BE

Sponsor information

Organisation
Brighton and Sussex University Hospitals NHS Trust (UK)

Sponsor details
Clinical Investigation and Research Unit (CIRU)
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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Brighton and Sussex University Hospitals NHS Charitable Fund (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2016		Yes	No
HRA research summary			28/06/2023	No	No