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Difficulty retrieving words (anomia) in people with relapsing-remitting multiple sclerosis (RR-MS)

Submission date
06/03/2018

Recruitment status
No longer recruiting

Registration date
15/03/2018

Overall study status
Completed

Last Edited
14/10/2022

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

BACKGROUND
Multiple sclerosis (MS) is one of the most common diseases of the central nervous system (CNS) and frequently starts in young adult life compared with other neurological conditions(Calabrese et al., 2009). This chronic immune system disease, characterised with the loss of myelin and destruction of nerves fibres, may involve neurons of any part of the brain or spinal cord and affects diverse functional systems including ambulation, vertigo, imbalance, fine motor, bladder, bowel, cognitive and speech communication abilities. (Noseworthy, Lucchinetti, Rodriguez, & Weinshenker, 2000). Physical disabilities accompanying the disease have typically been the focus of attention for physicians and patients. However, in the past decade, impairment in cognitive and speech communication has been significantly considered. Cognitive impairment is common and it is observed in approximately 40-70% of all subtypes and stages of the disease (Langdon et al., 2012). Furthermore, language problems and poor communicative capability are found in 40 - 60% of MS patients, negatively impacting their quality of life. Cognitive impairment in people with MS has only been recently studied. Moreover, only a limited amount of research has been focused on disordered language skills in people with MS (Laakso, K., Hartelius, & Ahlsén, 2000; Mackenzie & Green, 2009).
Communication skills in people with MS can be affected in different ways. For some people, dysarthria (impaired movements of the vocal cords, tongue, lips etc. causing speech to be unclear) is a problem . For others, changes in thinking skills for producing words quickly and easily can be affected. The incidence of anomia (difficulties retrieving a word) in people with MS is probably under-estimated, partly because symptoms can be subtle, and partly because we have no reliable tools with which to check for these problems within MS clinics. Patients with anomia find that the everyday words cannot be produced easily or quickly; in milder presentations, there may be delay in retrieval of infrequently accessed, more sophisticated vocabulary.
The precise nature and extent of cognitive-linguistic deficits such as anomia, in terms of the underlying impairments in thinking which cause behaviours such as lapses in word retrieval or inefficient, audible word searches, continues to be unclear.
Given the crucial role of verbal communication in everyday social, vocational and family life, it has been noted that even mild communication impairments lead to major lifestyle changes

characterized by substantial limitations in communicative participation (Yorkston, Klasner, & Swanson, 2001).

STUDY AIMS.
The present study is designed to help us understand the nature and extent of anomia (difficulties retrieving words) experienced by many people with MS. We are also interested in knowing how the symptoms of anomia affect MS patients' everyday functioning, and if a simple language therapy can affect the accuracy and efficiency of word retrieval. Understanding these issues is important if we are to develop more effective communication treatments.

WHO CAN PARTICIPATE?
50 people can take part of the study.
- Adults (>18 years old)
- Diagnosis of Relapsing-Remitting Multiple Sclerosis
- Native English speakers
- Have access to a laptop/tablet/PC to take part in treatment and homework exercises
- Do not have any metal implant in their body
- Not being pregnant

WHAT DOES THE STUDY INVOLVE?
The study first involves an interview at the MS out-patient clinic after the participant's appointment or at any time/date convenient to him/her. The participant will be asked to provide some information such as age, education, handedness and medical history (time of diagnosis). The research team will also access some sections of your medical history to confirm relevant information for the study. Then we will carry out some pen and paper tasks involving thinking skills such as memory, attention and naming. The testing will last up for 50 minutes.
The initial testing will provide us with information about their cognitive and naming skills which will help us decide if some participants meet our criteria to take further part in Phase II of the study. We will need 20 participants for Phase II. Suitable participants will be contacted for the follow-up study.
The follow up study consists on a various cognitive assessments (pen and paper thinking tasks) at the participants home which will take up to 4 hours and can be divided into 2 or 3 different sessions with 10-minute breaks to avoid fatigue. The same 20 participants will be invited to take a magnetic brain scan taking up to 70 minutes. Finally, we will give the 20 participants a computer-based language therapy consisting of 4 weekly pre-therapy tests, 10 weekly therapy sessions with a 6-week gap and 2 weekly post-therapy testing sessions. Each therapy session will last an hour. Therapy sessions can be the participants' home at a date/time convenient for them. The training will consist of using a computer program which we will provide in any technological device owned by the participant (such as computer, tablet or laptop). The program will generate specific target words that we hope will improve naming accuracy. The therapy is aimed to improve word retrieval skills.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF PARTICIPATING?
Participants may find taking part in the research interesting, satisfactory and enjoyable.
The research may not help the participant personally, but the information we get might help us understand anomia in MS more fully leading a better treatment in the future.
There may be a risk for some people of becoming bored or frustrated by taking part when assessing the cognitive functions or while in therapy, but that feeling will go away once the task stops and it will have no long term impact.
Participants may also find the Magnetic Resonance Imaging (MRI) scan machine very noisy, or feel uncomfortable. Ear protection such as noise-cancelling headphones will be provided and pillows to ensure they feel comfortable.

WHERE IS THE STUDY RUN FROM?
Participants will be recruited at the Salford Royal Foundation Trust (SRFT).
Brain scans will be taken at the Central Manchester University Hospitals NHS Foundation Trust (CMFT).
Data analyses will be performed at the University of Manchester

HOW LONG WILL THE TRIAL BE RECRUITING PARTICIPANTS FOR?
The recruitment times are from 01/10/2017 to 31/03/2018
The study is funded by the University of Manchester and the Mexican National Council for Science and Technology (CONACyT)

WHO IS THE MAIN CONTACT?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number
226347

ClinicalTrials.gov number

Secondary identifying numbers
IRAS project 226347

Study information

Scientific Title
Anomia in people with relapsing-remitting multiple sclerosis: investigating the nature and extent of the problem and taking steps toward better assessment and treatment.

Study objectives
Speeded naming therapy can help RR-MS patients manage anomia

Ethics approval required
Old ethics approval format

Ethics approval(s)
NHS Health Research Authorityn North East - Newcastle & North Tyneside 2 Research Ethics Committee, 13 September 2017, 17/NE/0242

Study design
Observational case-series cohort-observation cross-sectional study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Home

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Anomia in patients with relapsing-remitting multiple sclerosis

Interventions
PHASE I
The first phase will involve an interview and a one-time communication screening. It will be a 1:1 session..
In the interview participants will be asked their name, age, number of years diagnosed with MS, education in years, gender and whether they feel MS has affected their communication skills (ability to talk, remember words, produce sentences and understand others in conversation). Information will also be obtained from patient medical notes, such as corroboration of number of years since diagnosis, and measures of physical disability. Patient data will be recorded according to number recruited (no. 1, 2, 3…) and held in written and audio-recording format, pending data analysis.
The communication screening assessment can take place in either a room within Neurology out-patient department after their consultation or participants may agree to come back on another date, or at a subsequent out-patient appointment. If they feel more comfortable, the researcher can also visit them at their homes when it suits them.
The communication screening will measure divided attention, short and longer-term memory, categorising words and pictures according to meaning, generating lists of words in given categories, picture naming, using tests such as Addenbroke’s Cognitive Examination (ACE-R), Picture Naming Task (IPNP), National Adult Reading Test (IPNP) and Pyramids and Palm Trees.

All participants involved in the first phase will be given a consent to contact form in case they are invited back to participate in the second and third phase.
Patient data will be immediately anonymised according to number recruited (no.1, 2, 3…).
The screening assessment will help us understand both the extent and the nature of the problem of anomia in M.S. in the context of broader communication skills.
Communication screening: 35-45 min per participant.

PHASE II
In the second phase, after the data is analysed, 25 participants who show anomic symptoms of slow and or inaccurate word retrieval (from mildest to most severe), will be invited to continue to subsequent phases of the study. If the participants agree, they will be given a second consent form for the phase two and three.
Participants who consent to take part in the follow up study will take an in-depth neuropsychological assessment and a DTI scanning.
For the in-depth neuropsychological assessment the researcher will evaluate how useful traditional language tests which have stemmed from stroke aphasia (e.g. the Western Aphasia Battery) as well as widely-used cognitive assessments such as the Wisconsin Card Sort Test, Test of Everyday Attention, and Symbol Digits Modality Test. We will also establish which specific sub-sets of assessments of attentional/executive skills (e.g. Test of Everyday Attention - Robertson et al., 1994) are most sensitive to emerging processing deficits in these domains with participants with RR-MS. In total, neuropsychological assessment will take up to 240 minutes (4 hours) and this will be broken up into manageable units of time (e.g. 45-60 minutes) according to patient fatigue and convenience. Later we will set an appointment to carry out DTI scanning on the 25 participants with MS with no control participants without neurological diagnosis, as the range of anomic symptoms will serve as a form of experimental control against which the data from the scans is evaluated. Scanning the participants is a one-time task and it will last for around one hour, some months after the initial testing. The in-depth neuropsychological assessment and the DTI scan will be a few weeks away from each other.

PHASE III
The third part will be a treatment study with those 25 participants. The treatment phase will use simple therapy procedures with patient's available technology (computer, lap top, tablet) to support on-going self-management of the anomic symptoms and will be one weekly session over 24 weeks.
We will adapt a naming treatment that the supervisor Dr Paul Conroy has developed and evaluated with patients with stroke aphasia known as speeded naming therapy. This is based on training participants to become incrementally quicker at producing names for a set of trained words through use of everyday software displaying pictures like power-point. We will use 100 target words in the treatment and these will be matched with another 100 words of similar difficulty for each participant. The target words will be words for which each participant was either inaccurate or slow in naming at the baseline testing phase.

Target words will include words which were previously tested in phase 1 (symptom screen) and phase 2 (neuropsychological assessment). These will be familiar everyday words of varying frequency - e.g. high frequency - library; low frequency - microscope. Participants will also be able to suggest words of high personal relevance which they practically need on a day-to-day basis such as family members' names, and place names.
Treatment will therefore be adapted to each individual's vocabulary level, in terms of the types of words with which they experience anomic symptoms (e.g. people's names or technical vocabulary or everyday words etc.)
This will be a case-series neuropsychological therapy study, which means that the same testing

and treatment procedures are carried out across the sample of 25 participants with RR-MS, allowing a single case comparison (i.e. comparing 1 participant over time) and cross-case comparison (e.g. Comparing response to therapy in relation to anomic severity).

The treatment phase will take place in people's homes for 24 weeks consisting on weekly sessions over 24 weeks by the researcher.
Weeks 1 - 4 Pre-therapy testing: 4 weekly sessions. Baseline performance of 100-item confrontational naming test will be assessed three times to examine the stability of naming responses before therapy commences. We will also obtain brief discourse samples (e.g. 3-4 minutes of monologues on everyday topics like a recent holiday) to obtain a sample of word retrieval in everyday speech and measure linguistic features such as mean length of utterance, instances of word retrieval failure, adaptive behaviours in such instances etc.

These baseline data will be the pre-treatment measures against which post-treatment measures will be compared.

Weeks 5 – 14: Therapy 10 weekly sessions: The treatments will be delivered one session per week for ten weeks. Initially, the treatment is a standard supported naming treatment using verbal cues provided to participants. This is a well-established treatment protocol used across stroke and progressive diseases like primary progressive aphasia related to dementia and MS. The researcher presents pictures to be named and provided verbal cues to help this become more reliable. Initially, participants are asked to name each picture, presented on a computer screen, in 10 seconds without support, i.e. with no cues. After each naming attempt, feedback will be provided both verbally by the researcher and presented in writing on the screen. Initially, minimal cues will be provided (e.g. the initial consonant and vowel of the target word, e.g. “wi” for ‘window’) but the cues will be increased if naming is not achieved (next most of word, e.g. “wind” for ‘window’, and then the whole word ‘window’). Participants will work through all therapy items three times per session. As picture-naming accuracy improves (typically after 3-4 sessions) to an accuracy level of 75% of treated items, the treatment progresses to focus on enhancing the speed of naming responses, in other words making these shorter and more automatic for participants. This method, known as 'Repeated, Increasingly-Speeded Production' (RISP treatment), has been adapted from the so-called 'deadline naming' method used in experimental psycholinguistics research to assess the effect of speeded naming on speech production (Hodgson & Lambon Ralph, 2008; Vitkovitch & Humphreys, 1991). Participants will be instructed that the computer would present the picture for a limited amount of time and their task will be to try to name the picture before the beep at the end of the stimulus presentation. In each therapy session the presentation duration/time-to-the-beep will be reduced. Specifically, during each trial, the target picture will be presented on the computer screen for a fixed time. At the end of the allotted time, the picture will disappear and a beep sound will be produced by the computer. A blank screen will then be displayed for 1000msec. Participants will then be presented with the written target word on the screen as feedback and the correct spoken name of the picture will play by the computer. In the case of an incorrect response, the participant will be asked to repeat the correct name after the computer/experimenter three times. Participants will cycle through all therapy items three times per session.

Homework tasks will be suggested to allow independent practice outside of therapy sessions. The available technology will allow for monitoring of the frequency and duration of homework sessions.

Weeks 15-16: Post-therapy testing: 2 sessions immediately

Weeks 17 – 22: 6 week gap

Weeks 23-24: Follow-up post-therapy testing: 2 sessions to assess longer term maintenance and experience of self-management.

Post-therapy performance will be assessed for word-retrieval performance in picture naming and discourse samples. Both treated 100 and untreated 100 items are presented in random order using E-Prime software (Schneider, Eschman, & Zuccolotto, 2002) such that each picture will be presented simultaneously with an auditory beep and will remain on the screen for a maximum of ten seconds. Audacity software will be used to measure naming latencies by measuring the time elapsed from the beep to the onset of the participant's correct response.

Intervention Type
Behavioural

Primary outcome measure
The primary outcome for the study is the determination of the extent and nature of the problem of anomia in RR-MS measured as percentage naming accuracy on a bespoke naming test, and also changes on this naming test as a result of anomia treatment. .
The results for the extent of anomia in MS patients will be measured on participants global and individual performance on cognitive assessments and correlational and regression analyses with regard to linguistic or non-linguistic cognitive factors contributing to anomia severity.
The nature of anomia will be measured by analysing MRI data using probabilistic tract mapping and anatomical connectivity mapping.
Improvement of anomia symptoms will be measured using a case-series neuropsychological therapy study, allowing a single case comparison and cross-case comparison to therapy in relation to anomic severity.

Secondary outcome measures
The primary outcome measure will be interpreted in the context of participants' global and individual performance on cognitive screening using the Addenbroke's Cognitive Examination (ACE-R), the Picture Naming Task (IPNP), the National Adult Reading Test (IPNP) and Pyramids and Palm Trees (PPT) Test at baseline. Also correlational and regression analyses will be used to explore if other factors such as, time of diagnosis or number of relapses collected by reviewing the participant's medical records contribute to anomia.
The nature of anomia will be interpreted through in-depth neuropsychological assessment, along with the knowledge of the areas of the brain that have been affected by MS. A one-time MRI scan of each participant 3 months after the cognitive screening and an in-depth neuropsychological assessment including the Western Aphasia Battery (WAB), the Boston Naming Test (BNT), the Wisconsin Card Sort Test (WST), Test of Everyday Attention (TEA) and the Symbol Digits Modality Test (SDMT) within a week of the scan will be used. A probabilistic tract mapping and anatomical connectivity mapping will be conducted on the diffusion data to examine white matter tissue integrity. Both the lesion and white matter integrity measures will be related to performance using voxel based correlational methodology. The resting-state functional connectivity data will be processed via DPARSF (http://rfmri.org/DPARSF), and the resulting functional networks will be identified and examined in relation to both the behavioural and structural connectivity data.
MS lesions will be identified manually from the T1 and T2 scans for lesion-symptom mapping. In addition, probabilistic tract mapping and anatomical connectivity mapping will be conducted on the diffusion data to examine white matter tissue integrity. Both the lesion and white matter integrity measures will be related to performance using voxel based correlational methodology.

The resting-state functional connectivity data will be processed via DPARSF (http://rfmri.org/DPARSF), and the resulting functional networks will be identified and examined in relation to both the behavioural and structural connectivity data.

Overall study start date
01/01/2017

Completion date
01/06/2020

Eligibility

Key inclusion criteria
1. Diagnosis of RR-MS
2. English as a first language
3. Access to a laptop/tablet/PC to take part in treatment and homework exercises

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
50

Total final enrolment
13

Key exclusion criteria
1. Severe dysarthria (sufficient to make words produced unintelligible)
2. Cardiac pacemaker or defibrillator implanted
3. Insulin or infusion pump implanted
4. Cochlear, otologic, or ear implant
5. Any implant held in place by a magnet
6. Tissue expanders (plastic surgery)
7. Implanted catheter, clamp, clips, valves, or other metal
8. Tattoos or permanent makeup above shoulders
9. Shrapnel or metal fragments in body
10. Ever had metal removed from eye
11. Ever worked as a metal worker
12. Pregnant

Date of first enrolment
01/10/2017

Date of final enrolment

01/04/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Salford Royal Foundation Trust
Stott Lane, Salford
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M6 8HD

Sponsor information

Organisation
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Sponsor type
University/education

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
University/education

Funder Name
University of Manchester

Alternative Name(s)
The University of Manchester, University of Manchester UK, University of Manchester in United Kingdom, UoM

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Funder Name
Consejo Nacional de Ciencia y Tecnología

Alternative Name(s)
Consejo Nacional de Ciencia y Tecnología, National Council of Humanities, Sciences and Technologies, Mexican National Council of Science and Technology, National Council for Science and Technology (CONACyT), National Council of Science and Technology, Mexico, Conahcyt

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Mexico

Results and Publications

Publication and dissemination plan
The findings will be published as part of a doctoral degree.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
This will be made available on request, after publication of the thesis and associated manuscript publications.

IPD sharing plan summary
Available on request, Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			01/04/2019	No	Yes
Thesis results			14/10/2022	No	No
HRA research summary			28/06/2023	No	No