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Reconstructing sentence processing in aphasia

Submission date
05/09/2019

Recruitment status
No longer recruiting

Registration date
13/09/2019

Overall study status
Completed

Last Edited
04/08/2025

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
One consequence of a stroke can be aphasia – difficulty understanding and producing language. It limits a person's ability to take part in conversations. There has been considerable progress in vocabulary interventions for aphasia, but less in therapies for sentence processing. This is a problem as everyday talking involves sentences, and understanding and using sentences are critical for taking part in conversations. We apply a new theory of sentence processing to aphasia: usage-based construction grammar. In this intervention study, we test the effectiveness of a new computer therapy. It aims to improve understanding of spoken language and to stimulate flexible production of common phrases in everyday talking. The treatment involves listening to high-frequency phrases, and subsequent practice in producing those phrases with increasing flexibility as new vocabulary is inserted into the phrase.

We will measure language abilities twice before therapy starts to discover if behaviour is stable before intervention. All participants will then take part in 12 sessions of computer therapy spread over a period of 4 weeks. We then re-measure language abilities immediately after the therapy period and again after an 8 week period to determine the longer-term effects of the therapy.

Who can participate?
People with aphasia who have had a stroke at least 6 months ago, who previously were competent in speaking English. Participants must have sufficient visual and auditory acuity to interact with a computer.

What does the study involve?
Participants have to travel to University College London and complete 12 sessions of therapy in a 4 week period. Each session lasts for approximately 45-60 minutes. All participants will receive a new computer therapy aimed at improving sentence comprehension and production abilities. Participants will also complete a further 4 assessment sessions, two before the intervention and two after intervention. Language ability, linked cognitive skills and attitudes and feelings to life after stroke will be measured. Audio recordings of participants' speech will be made. Participants who meet MRI safety criteria will have two MRI brain scans, one in the pre-therapy phase and one at the end of the study.

What are the possible benefits and risks of participating?
The possible benefits of participating are that individuals will receive 4 weeks of intensive therapy which may lead to improved sentence understanding and production.

There are no known side effects associated with computer therapy. However, participants might not benefit from this therapy. During the intervention, there is the potential for some distress, as a participant is confronted with the loss of linguistic competence. MRI is not suitable for all people (e.g. people with metal implants). Furthermore, it may be unsuitable for people who are anxious in confined spaces, and some people do not like the sound of the scanner when it is in operation.

Where is the study run from?
The study is run from the Bloomsbury campus (Chandler House) of University College London (UK).

When is the study starting and how long is it expected to run for?
The study begins in September 2019 and will run until April 2023

Who is funding the study?
The Stroke Association.

Who is the main contact?
Professor Rosemary Varley
rosemary.varley@ucl.ac.uk

Study website
https://www.cognitionandgrammar.net/utilise

Contact information

Type(s)
Scientific

Contact name
Prof Rosemary Varley

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Reconstructing sentence processing in aphasia: Unification Therapy Integrating LexIcon and Sentences

Acronym
UTILISE

Study objectives
Current study hypothesis as of 21/10/2021:
1. Sentence therapy is more effective than usual care.
2. The effects of therapy are retained over an 8-week no-treatment period.

Previous study hypothesis:
1. Sentence therapy is more effective than usual care.
2. Outcomes of behavioural therapy are enhanced by active-anodal tDCS over left inferior frontal gyrus.
3. The effects of therapy are retained over an 8-week no-treatment period.
4. Maintenance is enhanced by active-anodal tDCS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 12/06/2019, UCL Research Ethics Committee (Office of the Vice Provost Research, 2 Taviton Street, University College London, WC1H OBW, UK; +44 (0)20 7679 8717; ethics@ucl.ac.uk), ref: 8123/001
2. Approved 20/06/2019, University College London Research Ethics Committee (2 Taviton Street, London, WC1H OBW, UK; +44 (0)20 7679 8717; ethics@ucl.ac.uk), ref: 8123/001

Study design
Single-centre randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
University/medical school/dental school, Other

Study type(s)
Treatment, Efficacy

Participant information sheet
http://www.cognitionandgrammar.net/s/Sentence_Therapy_Information_Sheet.pdf

Health condition(s) or problem(s) studied
Post-stroke aphasia

Interventions
Current intervention as of 21/10/2021:
After the initial baseline assessment, participants are randomised to 'immediate' or deferred treatment conditions. Randomisation: 1:1 immediate vs deferred (not stratified by sex), using block randomisation and random generation of 0/1 codes within each block. Researchers are blind to block size. Participants in the 'immediate' condition complete a second baseline assessment four weeks later and then immediately start the intervention. The intervention consists of a computerised behavioural intervention The computerised intervention comprises three tasks: attention to auditory sentence stimuli; attention to key components of sentence structure in a word monitoring paradigm; sentence production with gradual increase in sentence length and creativity. All stimuli include frequent phrase/sentence frames. The treatment is delivered in 12 x 45- to 60-minute sessions over a four week period.

Participants in the deferred condition will act as a waiting list control. They complete a second baseline assessment at eight weeks after the first baseline evaluation and then enter the intervention phase.

For both study arms, outcomes are measured immediately at end of the treatment phase and again after an eight-week no treatment/maintenance period.

Previous intervention:
After the initial baseline assessment, participants are randomised to 'immediate' or deferred treatment conditions, and active or sham transcranial direct current stimulation (tDCS). Randomisation is performed by an external randomisation service. Researchers and participants are blind to tDCS condition. Participants in the 'immediate' condition complete a second baseline assessment four weeks later and then immediately start the intervention. The intervention consists of a computerised behavioural intervention combined with active or sham tDCS. Stimulation is applied to the left inferior frontal region. Active stimulation parameters are 20 minutes at 1.5 mA. Sham stimulation comprises the same electrode montage, but, after initial ramp-up to 1.5 mA, stimulation is slowly decreased over 30 seconds. The computerised intervention comprises three tasks: attention to auditory sentence stimuli; attention to key components of sentence structure in a word monitoring paradigm; sentence production with gradual increase in sentence length and creativity. All stimuli include frequent phrase/sentence frames. The treatment is delivered in 12 x one hour sessions over a four week period.

Participants in the deferred condition will act as a waiting list control. They complete a second baseline assessment at eight weeks after the first baseline evaluation and then enter the intervention phase with randomisation to either active or sham tDCS.

For both study arms, outcomes are measured immediately at end of the treatment phase and again after an eight-week no treatment/maintenance period.

Intervention Type
Behavioural

Primary outcome measure
1. Sentence comprehension is measured using the Test for Reception of Grammar (TROG-2, Bishop, 2003).
2. Sentence production is measured using narrative speech evaluated by automated language analysis with the key variable of combination ratio (number of 3-word combinations/total number of words).
Primary outcome measures are completed twice at baseline to evaluate pre-intervention stability of behaviour. Assessments will be repeated immediately on cessation of treatment and after an 8-week no-treatment maintenance period.

Secondary outcome measures
1. The capacity to produce treated and matched control sentences is measured using a study-specific story completion test at Baseline 1 and immediately after the intervention.
2. Perceptions of quality of life are measured using SAQOL-39 at Baseline 2 and second /maintenance outcome (Hilari et al., 2003).
3. Sentence production is also evaluated using connected speech measures of mean length of utterance, function word ratio and frequency characteristics of word combinations at all four assessment time-points.

Overall study start date
01/03/2019

Completion date
21/04/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 09/03/2020:
1. Premorbid competence in English
2. Premorbidly right-handed
3. Single left hemisphere stroke
4. At least 6 months post-stroke onset
5. Presence of aphasia, characterized by spoken sentence comprehension impairment (scoring < 16 blocks correct on TROG-2) and/or spoken sentence production difficulties (incomplete and/or simple sentences) at baseline assessment
6. Capacity to give informed consent
7. Sufficient auditory and visual capacity to interact with the behavioural therapy

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Previous inclusion criteria:
1. Premorbid competence in English
2. Premorbidly right-handed
3. Single left hemisphere stroke
4. At least 6 months post-stroke onset

5. Presence of aphasia, characterized by spoken and written comprehension impairment and spoken sentence production difficulties
6. Capacity to give informed consent
7. Sufficient auditory and visual capacity to interact with the behavioural therapy

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
30

Total final enrolment
39

Key exclusion criteria
Current participant exclusion criteria as of 21/10/2021:
1. Significant other neurological disorder (e.g., neurodegenerative illness)
2. History of speech and language disorder prior to stroke (e.g., developmental dyslexia)
3. Current involvement in another therapy trial

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Previous participant exclusion criteria as of 09/03/2020:
1. Significant other neurological disorder (e.g., neurodegenerative illness)
2. History of speech and language disorder prior to stroke (e.g., developmental dyslexia)
3. Current involvement in another brain stimulation or behavioural therapy trial
4. Metal implants on/in head causing tDCS risk and heart pacemakers
5. History of severe headaches requiring treatment with medication other than simple analgesia
6. History of seizure in the past 6 months
7. Headscarf or hairstyle that prevents contact between electrode and skin
8. Skin abrasion/abnormality below the site of the electrodes
9. Adverse effects to previous tDCS or other brain stimulation techniques
10. Pregnant or likely to be pregnant

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Previous exclusion criteria:
1. Significant other neurological disorder (e.g., neurodegenerative illness)
2. History of speech and language disorder prior to stroke (e.g., developmental dyslexia)
3. Metal implants on/in head causing tDCS risk
4. Recurring headaches
5. History of seizure in the past 3 months
6. Current involvement in another brain stimulation or behavioural therapy trial

Date of first enrolment
18/09/2019

Date of final enrolment
03/11/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University College London
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Sponsor information

Organisation
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Sponsor type
University/education

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ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
Stroke Association

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 12/06/2023:
Protocol will be published in open science source by 01/12/2019
Pilot case series will be submitted for publication by 01/03/2020
Trial outcomes will be submitted for publication by 01/01/2024

Previous publication and dissemination plan from 21/10/2021 to 12/06/2023:
Trial outcomes will be submitted for publication. Study protocol published in open science source, see https://osf.io/j9udn/.

Previous publication and dissemination plan:
Protocol will be published in open science source by 01/12/2019
Pilot case series will be submitted for publication by 01/03/2020
Trial outcomes will be submitted for publication by 01/07/2022

Intention to publish date
01/04/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Rosemary Varley (rosemary.varley@ucl.ac.uk)
Type: anonymised profiling, baseline and outcome data of those participants who consented to data sharing
Time: 01/06/2024 for 10 years
With whom: researchers conducting meta-analyses
Mechanism: email contact with Rosemary Varley (PI) in the first instance
Consent: participants who gave explicit consent to anonymised data sharing

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	case series report	06/08/2021	21/10/2021	Yes	No
Protocol file	Study protocol addendum	20/10/2021	21/10/2021	No	No
Results article		11/07/2025	04/08/2025	Yes	No