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Retraining cognitive functions after epilepsy surgery in patients with hippocampal sclerosis

Submission date
07/12/2021

Recruitment status
No longer recruiting

Registration date
14/12/2021

Overall study status
Completed

Last Edited
13/12/2021

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The aim of this study is to find out whether cognitive retraining methods help to improve cognitive difficulties (e.g. with memory) in patients with epilepsy due to hippocampal sclerosis following surgery. Patients with seizures experience many difficulties and therefore may benefit from the surgery. Most patients are seizure-free after the surgery but they may experience some difficulties in day to day life such as remembering information or planning activities. Established cognitive retraining programmes to improve cognitive functions (such as memory, ability to plan and organize etc) will be used after surgery for seizures to see how they affect daily functioning. To study the changes in the brain, the researchers will be using a brain scanning method that does not cause any pain or harm.

Who can participate?
Patients from 16 to 50 years of age diagnosed as having hippocampal sclerosis who have been operated on between 6 months up to 7 years earlier, and are currently having no seizures. Similar age, gender and education matched healthy people with no history of brain disease or other medical conditions will also participate.

What does the study involve?
Participants will be randomly allocated into two groups, one that will undergo therapy and regular medication, and another that will continue on regular medication. Both the groups will be required to fill some simple questionnaires and undergo cognitive assessment/testing that will include tests for memory, attention, planning etc, requiring one session of 3-4 hours with a break in between. Also, all participants will be accompanied for a non-invasive (not causing any harm) brain scan. This will require one session. The therapy will consist of 18 1-hour daily sessions except for institute holidays and Sundays. These will consist of simple paper and pencil, oral/board-based tasks involving sorting/cancelling, learning a list of words etc, for improving attention, memory and planning abilities.
The group chosen to undergo regular medication will be required to come for re-assessment after 1 and 6 months and will be offered an opportunity to undergo retraining after the completion of the study.
After the completion of 18 sessions, all participants from both groups will undergo the same testing as first for 3-4 hours in a single session, along with another scan of the brain. Participants

will be required to come for follow up after 6 months for final testing again requiring 3-4 hours. The matched healthy group participants will have the same cognitive/brain functioning testing only once.

What are the possible benefits and risks of participating?
Participation in this research is entirely voluntary. Whether someone chooses to participate or not, all the services received at the hospital will continue and nothing will change. All participants are free to opt out of the research at any given point in time. The information collected from this study will be kept strictly confidential and will be used solely for research. There will be no monetary or other tangible benefits/risks associated with participation in the study.

Where is the study run from?
National Institute of Mental Health and Neurosciences (NIMHANS) (India)

When is the study starting and how long is it expected to run for?
July 2015 to February 2021

Who is funding the study?
Indian Council of Medical Research (ICMR) (India)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
13

Study information

Scientific Title

Effectiveness of cognitive retraining on neuropsychological, neuroimaging correlates and quality of life following epilepsy surgery: a randomized control study

Acronym
CRINHSATL-AH

Study objectives
1. There will be significant differences in neuropsychological variables post cognitive retraining in patients with hippocampal sclerosis (HS) following temporal lobe surgery
2. There will be significant differences in quality of life post cognitive retraining in patients with HS following temporal lobe surgery
3. There will be significant differences in depression and anxiety post cognitive retraining in patients with HS following temporal lobe surgery
4. There will be significant differences in DTI networks post cognitive retraining in patients with HS following temporal lobe surgery

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/08/2016, NIMHANS Ethics Committee (National Institute of Mental Health and Neuro Sciences, Institute of National Importance, P.B. No. 2900, Hosur Road, Bengaluru-560 029, India; +91 (0)80 26995004; chatur@nimhans.ac.in), ref: NIMH/DO/ETHICS SUB-COMMITTEE 29TH MEETING/2016

Primary study design
Interventional

Study design
Single-centre interventional non-blinded randomized controlled trial with follow-up

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Unilateral hippocampal sclerosis post standard anterior temporal lobe resection

Interventions
The present study is a randomized controlled study with follow up after 6 months. It consists of two study groups (the intervention group and the treatment as usual group [TAU]) and one comparison group of matched healthy volunteers from the community. The healthy controls are age, education and gender-matched with the final recruited intervention group participants.

Randomization is carried out in the form of allocation concealment and a random number table is used to generate two groups for N = 60. Randomization is done after the initial screening and selection with consent. The patients are divided into two groups - the intervention and the treatment as usual group. Standard methods of ensuring allocation concealment include sequentially numbered, opaque, sealed envelopes (SNOSE). Due to a reduction in the sample, the randomized lot till N = 30 is utilized and the numbers are later analyzed for distribution properties in both groups.

The intervention group are required to undergo 18 1-hour daily sessions of hospital-based cognitive retraining sessions. The treatment as usual group does not receive any retraining through both groups continue on their regular pharmacotherapy/medications as decided by the Neurology follow-up team. For the study, the consenting participants are kept on constant AED schedules from recruitment to follow-up to keep the medication effect constant.

The cognitive retraining module is adapted and modified to suit the needs of epilepsy patients from the CR package for head injury (Kumar & Rao, 1999) which consists of a rehabilitation program for attention, response inhibition and memory. The tasks newly included in the study are adapted from the clinical retraining activities being carried out with routine patients or are developed based on the theories pertaining to the specific domain being trained. The cognitive retraining programme encompasses various domains such as attention, memory and executive functioning, with a greater focus on direct retraining and strategic memory-based intervention. The complexity for attention tasks as well as for memory is progressively increased once the patient has achieved 80% accuracy over a period of 2-3 sessions. Also, the activities are gradually increased after the initial pace of the session is decided based on individual baseline performance in the first few tasks introduced. As the patient group is characterized by unilateral resection of either right or left ATL-AH, the package is selected/designed with methods focusing on retraining of deficits for both, based on the current body of research.

A strategic approach in form of flexible modes of retraining based on the strengths of the individual is followed. The tasks include computer-based tasks along with paper-pencil tasks or practised by oral presentation through the therapist. Distributed practice sessions for the above tasks are planned in progressively increasing interval periods for enhancing memory retrieval. Similarly, a dual-task paradigm is used for strengthening working memory, which is gradually introduced by the 7 or 9th session or depending upon the progression of the volunteer. The tasks are divided into attention/switching, executive functions - fluency and working memory, visuo-integration and memory – verbal, visuo-contextual and visuospatial.

Cognitive retraining tasks/activities
Attention training tasks are letter cancellation, mental manipulation, PASAT/serial addition-subtraction task. Except for the first, all other activities are intended to train the verbal working memory. Fluency training tasks are phonemic fluency task, category fluency and design fluency. Visual integration training is provided using a task involving integrating two figures learnt in a grid-like manner. The visuospatial working memory training tasks are a Pie-location task and a Pie-object location task, which are computer-based. The verbal learning and memory training task is word-list Strategic. The visual memory training tasks are Visual object location, Paired Recognition, Contextual encoding of pictures and Connecticons.

Intervention Type
Behavioural

Primary outcome(s)
1. Neuropsychological variables measured using a combination of selected subtests from the WMS III IND, NIMHANS Neuropsychological Battery for Adults and D-KEFS subtests at baseline, 20 days to 1 month, and 6 months from the last assessment
2. Quality of life measured using QOLIE-31 at baseline, 20 days to 1 month and 6 months from the last assessment
3. Mood states of anxiety measured using GAD-7 and depression using PHQ-9 at baseline, 20

days to 1 month and 6 months from the last assessment
4. Diffusion tensor imaging for a selected group of participants using 3T-MRI at baseline and 20 days to 1 month

Key secondary outcome(s)
1. Left versus right ATL-AH neuropsychological profiles measured using a combination of WMS III IND, NIMHANS Neuropsychology Battery for Adults and DKEFS subtests at baseline
2. Neuropsychological variables compared between the intervention group and the healthy control group using WMS III IND, NIMHANS Neuropsychology Battery for Adults and D-KEFS subtests to establish gains/deficits post retraining at baseline and after the intervention
3. Levels of cognitive estimation/subjective confidence levels in intervention and treatment-as-usual groups measured using subjective confidence ratings at baseline, 2nd assessment and follow-up

Completion date
04/02/2021

Eligibility

Key inclusion criteria
Patients:
1. Patients diagnosed with DRE with HS or dual pathology (FCD) within the resected area as determined by pre-surgical imaging and other neurological examinations from the neurosurgery inpatient and outpatient services of NIMHANS
2. Patients who have subsequently undergone ATL-AH and are stabilized on anti-epileptic drugs (AEDs) over a period of 6 months to 7 years post-surgery
3. Patients with 1A outcome of surgery on Engel's classification system
4. Patients within 18 to 50 years of age
5. Patients who are right-handed
6. Patients with at least the ability to read and write in one language
7. Patient with language fluency in Hindi, English or Kannada
8. Patients with adequate/corrected auditory, visual and/or motor function

Healthy controls:
1. Individuals matching with the Intervention group participants on gender, age and education within ±2 SD range
2. Individuals within 18 to 50 years of age
3. Individuals who are right handed
4. Individuals with and ability to read and write in one language
5. Individuals with language fluency in Hindi, English or Kannada
6. Individuals with adequate/corrected auditory, vision and sensory-motor functions

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
43

Key exclusion criteria
Patients:
1. Patients diagnosed as having double pathology or extra-temporal pathology
2. Patients who have undergone surgery before the age of 12 years
3. Patients who have undergone multiple surgeries for epileptic seizures or any other neurological condition
4. Patients with any outcome of seizure other than 1A on Engel's classification system
5. Patients with a history of intellectual disability
6. Patients who have undergone any form of psychological intervention
7. Patients with any other neurological, medical and psychiatric conditions including substance abuse

Healthy controls:
1. Individuals with a history of intellectual disability
2. Individuals who have undergone any form of psychological intervention.
3. Individuals with any other psychiatric (including substance abuse) and neurological conditions
4. Individuals with a history of medical conditions

Date of first enrolment
01/10/2017

Date of final enrolment
04/02/2021

Locations

Countries of recruitment
India

Study participating centre
National Institute of Mental Health and Neuro Sciences, Institute of National Importance
P.B. No. 2900, Hosur Road
Bengaluru
India
560 029

Sponsor information

Organisation

National Institute of Mental Health and Neurosciences

ROR
https://ror.org/0405n5e57

Funder(s)

Funder type
Research council

Funder Name
Indian Council of Medical Research

Alternative Name(s)
Indian Council of Medical Research, Government of India, Indian Council of Medical Research (ICMR), New Delhi, ICMROrganisation, , Indian Council of Medical Research, New Delhi, ..., ICMR, ICMRDELHI, ...

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
India

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date