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Defeating the giant with a slingshot: testing a new technology to fight the global trauma epidemic

Submission date
11/10/2017

Recruitment status
No longer recruiting

Registration date
12/04/2018

Overall study status
Completed

Last Edited
06/09/2021

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
For a variety of reasons, traumatic stress remains a global problem. Large segments of the population suffer from the after-effects of traumatic events, such as natural and man-made disasters and interpersonal violence. Given the debilitating and frequently long-term duration of the disorder, there is an unmet need to provide victims with effective and readily available treatments. This is particularly true in many developing countries, where treatment options are limited, despite the high frequency of certain types of trauma, notably torture. Reconsolidation blockade using the drug propranolol is emerging as a promising simple and inexpensive new treatment in psychiatry. The aim of this study is to compare the effectiveness of reconsolidation blockade to the current gold-standard treatment paroxetine to treat torture survivors from Nepal suffering from chronic post-traumatic stress disorder (PTSD).

Who can participate?
People between the ages of 25 and 65 who speak a Nepali language and have experienced a potentially traumatic event more than 6 months ago and show evidence of trauma-related distress, or impaired functioning, not present before the traumatic event

What does the study involve?
Participants are randomly allocated to one of two groups. One group receives the memory reconsolidation blockade treatment over 6 weeks (once per week), while the other group receives a 12-week paroxetine treatment. PTSD symptoms are assessed before and after treatment.

What are the possible benefits and risks of participating?
If successful, this study could help to demonstrate that reconsolidation blockade using propranolol could offer a fast and inexpensive solution to treating individuals suffering from PTSD across the world. The main potential benefit for participants of the study is the treatment of PTSD symptoms. Risks of taking propranolol include congestive heart failure, AV block and bronchial asthma (all very uncommon in properly screened participants). Side effects include hypotension, tingling, numbness, light-headedness, tiredness, weakness, depression, sexual

impotence, hallucinations, vivid dreams, disorientation, short-term memory loss, nausea, vomiting, cramps, diarrhea, constipation, sore throat, rash, and fever. Side effects of propranolol are short-lasting, reversible, and do not require stopping the medication. The researchers have been using propranolol since 2004 and have treated hundreds of patients with virtually no complications. The negative side-effects for individuals who use paroxetine are: asthenia (12%), nausea (18%), diarrhea (11%), dry mouth (10%), somnolence (16%), ejaculatory disturbance (13%), and other male genital problems (9%). Weight gain has also been noted. Most negative events depend on the dosage and tend to occur early in treatment. Using a dose of 20 mg will reduce such side effects without compromising how well the medication works.

Where is the study run from?
This study is run from both the Douglas Mental Health University Institute (Verdun, QC, Canada) and the Center for Victims of Torture (Dharan, Nepal). Participant recruitment and treatment, however, only takes place in Nepal at the Center for Victims of Torture

When is the study starting and how long is it expected to run for?
October 2012 to February 2019

Who is funding the study?
Grand Challenges Canada

Who is the main contact?
Dr Alain Brunet

Contact information

Type(s)
Public

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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
PRPL005

Study information

Scientific Title
Pre-reactivation propranolol therapy to reduce post-traumatic stress disorder in Nepalese torture survivors

Study objectives
Objective 1: To test the feasibility of conducting reconsolidation blockade interventions with propranolol as a treatment for PTSD in Nepali torture survivors
Objective 2: To determine whether the therapeutic effects of reconsolidation blockade with propranolol on PTSD symptom severity is comparable to paroxetine treatment

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Douglas Institute Research Ethics Board, 06/02/2013, ref: 12/41
2. Tribhuvan University Teaching Hospital, 30/01/2013

Study design
Single-center randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied

Post-traumatic stress disorder

Interventions
This study aims to compare how well the memory reconsolidation blockade therapy works when compared to the current gold-standard in PTSD treatment: a selective serotonin reuptake inhibitor called paroxetine. In order to do this, participants will randomly be assigned to one of two groups: one will receive the memory reconsolidation blockade treatment over 6 weeks, while the other will receive a 12-week treatment by means of paroxetine.

Participants are randomized to one of the two treatment conditions according to a double-blind randomization schedule that was prepared by personnel who were not otherwise involved in the study. A block randomization schedule was used to randomize subjects into groups that result in equal sample sizes. This method was used to ensure a balance in sample size across groups over time. Block sizes were balanced with the predetermined group assignments, with a 50% probability of being assigned to either the paroxetine or propranolol group.

For the paroxetine arm, the dosage will be 20mg per day via oral administration. Participants receiving paroxetine will be treated for a 12-week period during which they will receive paroxetine once daily. However, participants who wish to continue can receive paroxetine for 3 more months.

The 6-week (once per week) reconsolidation memory blockade treatment consists of a dose of 1 mg/kg of propranolol, a synthetic beta-adrenergic receptor blocker, administered 90 minutes before a reading of the script describing the individual's traumatic experience. Propranolol is administered orally.

A 26-week post-baseline follow-up assessment will be conducted for all subjects. The total duration for the final follow-up for all treatment arms is 5 years.

Intervention Type
Mixed

Primary outcome measure
The feasibility of memory reconsolidation blockade, measured by numbers of treatment completers, study adherence, and percentage of psychometric ratings completed, measured at one year after the recruitment start date

1. Traumatic events experienced, assessed using the clinician-administered PTSD scale (CAPS)-Trauma list at the first visit
2. Recalled peritraumatic responses, measured using the Peritraumatic Distress Inventory
3. PTSD symptoms, assessed using the self-report PTSD symptom checklist (PCL) prior to each traumatic memory reactivation session to cover the week elapsed since the last such session

Secondary outcome measures
1. Axis I morbidity and comorbidity: general psychiatric comorbidity measured with the Nepali version of the Hopkins Symptom Checklist. The WHODAS-2 is a disability assessment instrument based on the conceptual framework of the International Classification of Functioning, Disability, and Health. It will provide a global measure of disability and seven domain-specific scores. These measures will be taken prior to the treatment and after the 6-week treatment has been completed.
2. Global clinical improvement associated with changes in mental health status, assessed at each

visit with the Clinical Global Impression scale prior to treatment, at every treatment session (once per week for 6 weeks), and after the treatment has been completed
3. Quality of life, assessed using the WHO Quality of Life-BREF prior to the intervention and after the intervention has been completed

Overall study start date
01/10/2012

Completion date
01/02/2019

Eligibility

Key inclusion criteria
1. Male or female 25-65 years old
2. Fluency in a Nepali language
3. Having experienced a potentially traumatic event according to the CAPS trauma list more than 6 months ago
4. Evidence of trauma-related distress, or impaired functioning, not present before the index event
5. Evidence that the candidate participant understands the study procedures
6. Signed informed consent form, OR a document signed by the site principal investigator attesting that consent was given orally in the presence of a witness

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
50

Total final enrolment
46

Key exclusion criteria
1. Resting heart rate < 60 Beats Per Minute
2. Resting systolic blood pressure < 100 mm Hg
3. A PCL score below 50.
4. A CGI severity score below 4 (Moderately ill)
5. Not meeting the criteria for chronic PTSD at the time of randomization (visit 2)
6. Currently suicidal (i.e. a score of 3 or 4 on item 7 on the HSCL) or homicidal
7. A history of congestive heart failure, hypoglycemic medication-requiring diabetes, chronic bronchitis, emphysema, or asthma
8. Acute morbidity that leads to disabilityand that requires immediate medical treatment (e.g., gastric acid disease)

9. Previous adverse reaction to a β-adrenergic blocker
10. Presence of drugs of abuse, viz., alcohol, opiates, marijuana, cocaine, or amphetamines, as determined by collateral informants
11. Women of child-bearing potential who are not using an acceptable birth-control method, including abstinence (condoms will be provided for free)
12. Positive pregnancy test
13. Breastfeeding
14. Contra-indicating neuropsychiatric condition, e.g., current psychotic, bipolar, melancholic, memory problems or substance dependence or abuse disorder
15. Current use of medication that involve potentially dangerous interactions with propranolol, including, other β-adrenergic blockers, anti-arrythmics, and calcium channel blockers
16. Potent P450 2D6 inhibitors will not be exclusionary, because participants will receive only a single day's dose of propranolol under observation, so that build-up of plasma levels over time due to decreased metabolism will not be a problem
17. Current use of a medication that may involve potentially dangerous interactions with paroxetine, such as cimetidine, amitriptyline, desipramine, risperidone, atomoxetine, thioridazine, a MAOI, or pimozide

Date of first enrolment
01/04/2013

Date of final enrolment
01/02/2014

Locations

Countries of recruitment
Nepal

Study participating centre
Center for Victims of Torture
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Sponsor information

Organisation
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Sponsor type
University/education

Website
http://www.douglas.qc.ca/

ROR
https://ror.org/05dk2r620

Funder(s)

Funder type
Government

Funder Name
Grand Challenges Canada

Alternative Name(s)
Grands Défis Canada, GCC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Publication and dissemination plan
The study protocol will not be available. There is no statistical analysis plan. There are plans for initial publication of the first phase of the trial (treatment phase) in 2018. This publication will be exploring the feasibility and efficacy of the memory reconsolidation blockade treatment for PTSD.

Intention to publish date
01/06/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Alain Brunet. The data will become available after the first publication (envisioned for June 2018). Regarding access criteria, data will be shared with principal

investigators affiliated with a scientific or educational institution, with no specifications on the type of analyses. Informed consent from the participants was obtained, and their identity in the dataset is anonymous. There are no ethical or legal restrictions associated with this study.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		03/09/2021	06/09/2021	Yes	No