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OxLith: exploration of the short-term physical and psychological effects of lithium in mood instability

Submission date
20/01/2015

Recruitment status
No longer recruiting

Registration date
21/01/2015

Overall study status
Completed

Last Edited
16/06/2022

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Bipolar disorder affects around 2% of the world's population. Symptoms typically start in adolescence/early adulthood and persist throughout life. Bipolar disorder is usually characterised by manic and depressive episodes but recent studies have highlighted the long-term social and functional impairment associated with inter-episode mood instability. Evaluation of current treatments and the development of more effective, safer treatments could greatly improve the lives of people with bipolar disorder. Lithium is recommended for long-term prevention of mania and depression. It is an effective drug which reduces suicidality. However, lithium has a narrow therapeutic range and the adverse effects include changes in kidney, thyroid and parathyroid function. Despite having been prescribed for over five decades there is little understanding of the mechanism of action of lithium. Evaluation and development of treatments for mental illnesses have been hampered by the lack of robust measures of effect. New technologies offer ways to identify biomarkers that measure effects and elucidate mechanisms of action. These include electronic rating systems, brain imaging techniques, activity and sleep monitors, hormone level assays and cognitive function tests. In this study we will use these technologies to explore the mechanism of action of lithium.

Who can participate?
Men and women aged 18 or over who have bipolar disorder and are currently experiencing mood instability but not an episode of depression, mania or hypomania.

What does the study involve?
Following a 2-week run-in phase (during which no treatment is given), participants are randomly allocated to take either lithium or placebo for 6 weeks. During the time they are in the study participants are asked to rate their mood weekly by email or text message and to complete daily tasks on an iPad (provided). The daily tasks include cognitive tests assessing reaction times and learning and completing brief ratings of mood. Participants are also asked to carry activity monitors, wear a heart monitor for two 3-day periods, to give blood, saliva and cheek swab samples, and to have two non-invasive brain scans.

What are the possible benefits and risks of participating?
For the time that they are in the study, participants will benefit from consultations with psychiatrists who are experts in the treatment of bipolar disorder. Lithium can cause adverse effects. Common effects are upset stomach, particularly at the start of treatment, fine shake ('tremor') of the hands, metallic taste, increased thirst and need to pass urine and weight gain. Adverse effects will be monitored during the trial. The study does require daily completing of self-reports and cognitive tests as well as a number of clinic visits, two scans and two 32-hour periods of 4-hourly collection of saliva and cheek swabs. The frequency and timing of data collection and visits has been kept to a minimum and the study requirements will be made clear to all participants prior to consent.

Where is the study run from?
The study is being run by a team from the Oxford Cognitive Health and Neuroscience Clinical Trials Unit (OCHNCTU) based at the University of Oxford Department of Psychiatry. Participants will be recruited from the Oxford Health NHS Foundation Trust.

When is the study starting and how long is it expected to run for?
April 2015 to April 2017

Who is funding the study?
The study is funded as part of an award from the Wellcome Trust for CONBRIO, a programme of research designed to transform understanding and treatment of bipolar disorder.

Who is the main contact?
Dr Jennifer Rendell
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Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2014-002699-98

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CB001-OL

Study information

Scientific Title
OxLith: exploration of the short-term physical and psychological effects of lithium in mood instability

Acronym
OxLith

Study objectives
Aim: to characterise the clinical, cognitive, neural and pathophysiological effects of lithium in people with bipolar disorder and current mood instability.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central - Oxford A, 04/04/2015, ref: 15/SC/0109

Study design
Randomised 6-week double-blind placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

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
Bipolar disorder with current mood instability

Interventions
Following a 2-week run-in phase, participants will be randomly allocated to take either lithium or placebo for 6 weeks. During the time they are in the study participants will be asked to rate their mood weekly by email or text message and to complete daily tasks on an iPad (provided). The daily tasks will include cognitive tests assessing reaction times and learning and completing brief ratings of mood. Participants will also be asked to carry activity monitors, a heart monitor for two 3-day periods, to give blood, saliva and cheek swab samples, and to have two non-invasive brain scans.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Lithium

Primary outcome measure
Reduction in mood instability from weekly self-reports made online or by SMS throughout the trial (https://truecolours.nhs.uk). Depressive symptoms will be reported using the Quick Inventory of Depressive Symptoms (QIDS-SR16) scale and manic symptoms using the ALTMAN scale. Daily self-reports of current mood reported using the (Positive and Negative Affect Scale (PANAS) completed on an iPad

Secondary outcome measures
1. Performance on cognitive tasks at trial entry and at the final visit and on brief tasks completed daily on an iPad throughout the trial
2. Data on the way information is processed in the brain using magnetic resonance imaging (MRI) and magnetoencephalography (MEG) scans during week 4
3. Actigraphy data collected on small devices worn on the wrist or attached to clothing continuously throughout the trial to provide information on activity levels and sleep patterns

4. Changes related to circadian rhythms measured from cheek swabs and saliva samples which participants will collect at intervals over two 32-hour periods, one prior to entry to the randomised phase and the second during week 4
5. Changes in blood levels of biomarkers for related to adverse effects of lithium from blood samples taken at trial entry and at the final trial visit. Two additional blood samples will be taken in the first 2 weeks following randomisation to check lithium levels

Overall study start date
01/04/2015

Completion date
01/04/2018

Eligibility

Key inclusion criteria
1. Willing and able to give informed consent to participate in the trial
2. Meeting criteria for bipolar disorder
3. Clinical complaint of significant mood instability
4. Clinical uncertainty about the prescription of lithium
5. No clear indication for alternative treatment
6. Pre-treatment blood test results acceptable for initiation of lithium
7. Willing and able to comply with all trial requirements (assessed by a psychiatrist)
8. Willing to allow his or her General Practitioner and, if appropriate, psychiatrist to be notified of participation in the trial

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
40

Key exclusion criteria
1. Any contraindication to lithium
2. Currently taking any psychotropic drug that cannot be withdrawn
3. Clinically significant alcohol or substance use
4. Requiring immediate treatment for an acute mood episode such that placebo would be inappropriate
5. Female and pregnant, lactating or currently planning a pregnancy
6. Female of child-bearing potential not willing to use effective contraception
7. Participation in another research trial involving an investigational medicinal product in the past 12 weeks

8. Judged to be at significant immediate risk of suicide/self-harm
(Participants with contraindication to one or both brain scans will be excluded from that part of the trial)

Date of first enrolment
01/04/2015

Date of final enrolment
01/02/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Oxford Health NHS Foundation Trust
Warneford Hospital
Warneford Lane
Headington
Oxford
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OX3 7JX

Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
Joint Research Office
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Churchill Hospital
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Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The main results of the trial will be published together in an appropriate journal and made available to participants via the Department of Psychiatry website. Additional results from the individual themes will be published in topic-specific journals.

Intention to publish date
01/01/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. John Geddes.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	02/03/2016		Yes	No
Basic results		16/03/2022	16/06/2022	No	No
Basic results		16/03/2022	16/06/2022	No	No

HRA research summary	28/06/2023	No	No