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How does oxytocin affect brain functioning in people at high risk of developing psychosis?

Submission date
15/03/2023

Recruitment status
No longer recruiting

Registration date
17/03/2023

Overall study status
Completed

Last Edited
03/04/2023

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
Psychotic disorders are usually preceded by a prodromal phase, called the Ultra High-Risk Mental State (UHR), characterised by attenuated psychotic symptoms, emotional dysregulation and difficulties with interpersonal relationships. Emotional and social cognition problems are common in UHR individuals, are the main source of their distress, and are a key factor in the associated loss of vocational function. Administration of oxytocin (OT) appears to promote social interactions and emotional bonding in healthy volunteers, improve emotional and social dysfunction, and ameliorate psychotic symptoms in patients with schizophrenia. The present study will evaluate the mechanism of action of OT on social cognition and emotional processing in UHR individuals.

Who can participate?
Adults aged 18-35 who are UHR for psychosis.

What does the study involve?
During each OT/placebo challenge, the team will use magnetic resonance imaging (MRI) to measure the effects of OT on the neural substrates of emotional processing and social cognition. Subjects will also undergo a clinical assessment with standardized psychometric scales.

What are the possible benefits and risks of participating?
Participants will not benefit directly but the potential findings from the research may improve understanding of the neurobiological factors underlying psychosis. The experimental treatment will not interfere with the standard care of the participants. OT has been widely used for several years in medicine. A review of 38 studies conducted since 1990 with a total of 1529 participants indicated that 18-40 IU OT is safe. There is a risk that some participants may feel anxious or claustrophobic during MRI scanning.

Where is the study run from?
Department of Psychosis Studies at the Institute of Psychiatry, Psychology and Neuroscience, King’s College, London (UK)

When is the study starting and how long is it expected to run for?
January 2014 until October 2017

Who is funding the study?
1. National Institute for Health Research (NIHR) Biomedical Research Centre (BRC) at South London and Maudsley NHS Foundation Trust and King's College London
2. Brain & Behaviour Research Foundation National Alliance for Research on Schizophrenia & Depression (NARSAD) Award

Who is the main contact?
Prof Paolo Fusar-Poli, paolo.fusar-poli@kcl.ac.uk (UK)

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
150687

Protocol serial number
CPMS 18011, IRAS 150687

Study information

Scientific Title

Neurophysiological basis of effects of oxytocin on emotional processing and social cognition in people at ultra-high risk for psychosis.

Study objectives
The primary outcome measure is to investigate the regional brain response under oxytocin challenge (versus placebo) in subjects at ultra-high risk (UHR) for psychosis. Specifically, we hypothesise that a single dose of oxytocin modulates brain functioning during emotional processing and social cognition in UHR subjects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/11/2014, London – London Bridge Research Ethics Committee (Research Ethics Committee London Centre, Ground Floor, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)207 1048 387, (0)207 1048 124; londonbridge.rec@hra.nhs.uk), ref: 14/LO/1692

Study design
Randomized interventional study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Schizophrenia, schizotypal and delusional disorders

Interventions
This is a randomised, double-blind, 40 IU intranasal oxytocin versus placebo single-dose challenge with a crossover design (1-week washout). Oxytocin administration will follow international guidelines (Guastella AJ et al., Recommendations for the standardisation of oxytocin nasal administration and guidelines for its reporting in human research) and be conducted under researcher supervision. During each challenge, subjects will undergo a 90-minute MRI scan which includes fMRI tasks exploring social cognition, arterial spin labelling, resting-state fMRI, and MR-spectroscopy.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

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

Primary outcome(s)

Regional brain response to oxytocin versus placebo challenge in subjects at ultra-high risk (UHR) for psychosis measured using MRI, which includes fMRI tasks of social cognition and other neuroimaging readouts (arterial spin labelling, resting-state fMRI, and MR-spectroscopy), during the challenge

Key secondary outcome(s))
The are no secondary outcome measures

Completion date
17/10/2017

Eligibility

Key inclusion criteria
Among the new referrals to the OASIS service, South London and Maudsley NHS Foundation Trust, we will enroll those meeting inclusion criteria for a UHR state for psychosis (as defined on the CAARMS revised version questionnaire).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Male

Total final enrolment
30

Key exclusion criteria
1. Personal history of psychotic illness (i.e. schizophrenia, schizoaffective disorder or related psychosis)
2. Aged below 18 years old
3. Aged over 35 years old
4. Significant cognitive deficit (IQ<60 as measured by the shortened WAIS)
5. Significant history of drug or alcohol misuse or dependence
6. Severe neurological and medical conditions
7. Evidence of hyponatremia in participant's recent blood test
8. Rejection of informed consent
9. Pregnancy (apply to women of childbearing age)
10. Breastfeeding (applies to women of childbearing age)
11. Non-use of contraceptive methods (apply to women of childbearing age).

Date of first enrolment
06/05/2015

Date of final enrolment
10/10/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Kings College London
Strand
London
United Kingdom
WC2R 2LS

Study participating centre
Maudsley Hospital
Denmark Hill
London
United Kingdom
SE5 8AZ

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park
Denmark Hill
London
United Kingdom
SE5 8AB

Study participating centre
East London NHS Foundation Trust
Robert Dolan House
9 Alie Street
London
United Kingdom
E1 8DE

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Organisation
South London and Maudsley NHS Foundation Trust

ROR
https://ror.org/015803449

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Brain and Behavior Research Foundation

Alternative Name(s)
Brain & Behavior Research Foundation, The Brain & Behavior Research Foundation, Brain & Behavior Research FDN, The Brain and Behavior Research Foundation, BBRFoundation, National

Alliance for Research on Schizophrenia & Depression, NATIONAL ALLIANCE FOR RESEARCH ON SCHIZOPHRENIA AND DEPRESSION, National Alliance for Research on Schizophrenia and Depression, Inc., BBRF, NARSAD

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available. Individual-level data are not currently openly available due to data privacy, ongoing research and regulatory/ethical approvals. However, aggregate (group-level) clinical, demographic and imaging data may be made available, upon request (at the investigator's discretion) via contact with Prof Fusar-Poli, paolo.fusar-poli@kcl.ac.uk. Aggregate data have already been shared with, for example, the ENIGMA Clinical High-Risk Working Group for the purposes of large-scale cross-site meta- and mega-analysis.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Oxytocin modulates hippocampal perfusion	09/01/2019	15/03/2023	Yes	No
Results article	Oxytocin on brain activation during inferring others' beliefs and social emotions	22/06/2020	15/03/2023	Yes	No
Results article	Oxytocin on glutamate and other metabolites	28/03/2019	15/03/2023	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Intranasal oxytocin increases heart-rate variability in men at clinical high risk for psychosis: a proof-of-concept study	12/07/2020	15/03/2023	Yes	No