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Brain imaging of the adenosine A2A receptor in schizophrenia

Submission date	Recruitment status	[X] Prospectively registered
03/02/2014	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
10/02/2014	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
15/05/2018	Mental and Behavioural Disorders	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Schizophrenia is a mental disorder affecting nearly 1% of the population. An imbalance of chemicals in the brain is thought to be the major cause of the disease. As a result, multiple factors have been associated with the disorder and evidence from post-mortem patient brains often guide research in understanding this disorder. One such protein known as the adenosine A2A receptor (A2AR) has been reported to increase up to 70%. We want to first measure whether such an increase exists in living patients and secondly we want to rule out the role of antipsychotic medication contributing to this increase. To do so we will employ a specific molecule (a radiotracer which has been previously used in human subjects) that can be labelled with a small amount of radioactivity and imaged using positron imaging tomography (PET).

Who can participate?
Men aged 20-55 years old, including both healthy volunteers and patients with a diagnosis of schizophrenia.

What does the study involve?
The A2A receptor levels in the brain will be estimated using a PET radiotracer. Each subject will undergo a single PET and MRI scan. The MRI scan will provide brain structural information to map the radioactive tracer signal imaged by the scanner. Six un-medicated and six medicated subjects diagnosed with schizophrenia will be compared to six age-matched healthy volunteers. We have a database of 12 healthy volunteers previously examined with the PET radiotracer and if adequate age-matched healthy volunteer data sets are not available, we will recruit up to six healthy volunteers to carry out the comparison.

What are the possible benefits and risks of participating?
There are no direct benefits to volunteers participating in the study. However, information from the study will help design new therapies targeting the A2A receptor to treat schizophrenia. Arterial/venous cannulation and blood sampling can cause local bruising and infection. The major risk due to PET scans is the risk of exposure to radiation.

Where is the study run from?
The initial screening of healthy volunteers and patients will be done at the Institute of

Psychiatry, Kings College London (Denmark Hill Campus), UK. The brain scanning will be done at IMANOVA Ltd, Hammersmith, London, UK.

When is the study starting and how long is it expected to run for?
The study is expected to start recruiting healthy volunteers and patients from April 2014 and we expect to complete the study by March 2016.

Who is funding the study?
Kings College London is funding the study. IMANOVA Ltd has waived the cost of scanning under its pilot scheme to promote young researchers.

Who is the main contact?
Dr Eugenii (Ilan) Rabiner
eugenii.1.rabiner@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Eugenii Rabiner

Contact details
Dept. of Neuroimaging, PO Box 89
Institute of Psychiatry
King's College London
De Crespigny Park
London
United Kingdom
SE5 8AF
+44 (0)20 8008 6042
eugenii.1.rabiner@kcl.ac.uk

Additional identifiers

Protocol serial number
Ver 1.1 dated 04/11/2013

Study information

Scientific Title
A pilot positron emission tomography study to assess striatal adenosine A2A receptor expression in schizophrenia

Study objectives
Postmortem brains of patients diagnosed with schizophrenia have shown to express up to 70% increase in a protein known as adenosine A2A receptor. It is possible that antipsychotic medication could also have contributed to this increase. We want to understand this better by non-invasive PET imaging using a radiotracer selective to this receptor and by contrasting un-

medicated patients with medicated patients in comparison to baseline values exhibited by healthy subjects. The main questions that are being addressed are:
1. Is there an increase in adenosine A2A receptor expression in the living brain of patients diagnosed with schizophrenia?
2. Does antipsychotic medication contribute to its increased expression?

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - West London & Gene Therapy Advisory Committee (GTAC), 12/02/2014, Ref: 13/LO /1918

Primary study design
Interventional

Study design
Open labelled non-randomized study

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Schizophrenia

Interventions
Six un-medicated and six medicated subjects diagnosed with schizophrenia will be compared to six age-matched healthy volunteers. The quantification parameters for A2A receptor availability will be estimated using the PET radiotracer [11C]SCH442416. Each subject will undergo a single PET and MRI scan.

The A2A receptor availability of the patients with schizophrenia will be compared to a database of 12 healthy volunteers previously examined with [11C]SCH442416, and available at IMANOVA. If adequate age-matched healthy volunteer data sets are not available then up to six healthy volunteers will be recruited and will undergo one PET and MRI scan.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
VT (the total volume of distribution) of the radiotracer, which reflects the receptor availability in brain regions of interest, will be determined to help us evaluate the difference in receptor distribution among the groups that are being compared. This primary outcome is a single time-point measure obtained after PET scanning is completed.

Key secondary outcome(s)
No secondary outcome measures

Completion date
31/03/2016

Eligibility

Key inclusion criteria
All participants:
1. Male 20-55 years old
2. Adequate command of English to understand the information leaflet
3. Capacity to consent to participation in the study
4. Allens test showing adequate collateral circulation to the hand
5. Normal blood coagulation test

Healthy volunteers:
1. Eligibility determined by the responsible physician based on a medical evaluation including medical history, physical and psychiatric history

Schizophrenia patients (un-medicated):
1. Confirmation of DSM-V diagnosis for schizophrenia or schizophreniform disorder
2. At least one rating of moderate severity (PANSS ≥4) on the PANSS positive scale
3. Patients including first episode psychosis who have the capacity to make decisions about their clinical care and have chosen to abstain from antipsychotic medication
4. Patients who have had antipsychotic medication in the past must have voluntarily abstained from antipsychotic medication for at least 6 weeks

Schizophrenia patients (medicated):
1. Confirmation of DSM-V diagnosis for schizophrenia or schizophreniform disorder
2. At least one rating of moderate severity (PANSS ≥4) on the PANSS positive scale
3. Patients should be clinically stable in a non-acute phase for at least four weeks prior to the screening visit
4. Treatment with stable doses of atypical antipsychotics (except clozapine) for at least 12 weeks

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
Male

Key exclusion criteria
All participants:
1. Males aged less than 20 years and over 55 years
2. Women of all ages
3. Evidence or history of clinically significant hematological, renal, urinary/prostatic, endocrine, dermatological, pulmonary, psychiatric (except for diagnosis indicated in the inclusion criteria for schizophrenia patients), gastrointestinal, cardiovascular or other heart disease, glaucoma,

diabetes, hepatic, neurologic, head trauma or allergic disease (except for untreated, asymptomatic, seasonal allergies at time of dosing), if any, and in the opinion of the recruiting physician will impair the safety of the subject and/or the scientific integrity of the study
4. History of sensitivity to any of the study medications, or components thereof, or a history of drug or other allergy that in the opinion of the investigator puts them at risk
5. Significant history and continuing substance (except nicotine) and alcohol abuse
6. Heavy smokers > 20 cigarettes per day
7. Taking anti-asthmatic medication and any other concurrent medication including mood stabilizers, antidepressant or anti-cholinergic medication the physician may feel is contraindicated for the study
8. Subjects consuming > 500 mg per day of caffeine, which roughly equates to 5 cups of tea or coffee, 8 cans or five 20-ounce bottles of cola
9. Participation in a clinical trial and having received an investigational product within the time period mentioned prior to the first dosing day in the current study: 90 days, 5 half-lives or twice the duration of the biological effect of the investigational product (whichever is longer)
10. Exposure to more than four investigational new chemical entities within 12 months prior to the study
11. Donation of blood or blood products in excess of 500 ml within any 60-day period prior to the present study
12. Previous inclusion in a research and/or medical protocol involving nuclear medicine, PET or radiological investigations with significant radiation burden (a significant radiation burden being defined as ICRP category IIb or above: no more than 10 mSv in addition to natural background radiation, in the previous 12 months, including the dose from this study)
13. History of, or suffers from, claustrophobia or feels that they will be unable to lie still on their back in the MRI or PET scanner for a period of 2 hours
14. Presence of a cardiac pacemaker or other body implants that are ferromagnetic as assessed by a standard pre-MRI questionnaire

Date of first enrolment
01/04/2014

Date of final enrolment
31/03/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College London
London
United Kingdom
SE5 8AF

Sponsor information

Organisation
King's College London (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
University/education

Funder Name
King’s College London

Alternative Name(s)
King's, Collegium Regium apud Londinenses, Collegium Regale Londinense, Collegium Regale Londiniense, KCL

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Funder Name
Imanova Ltd (UK) - has waived the cost of scanning under its pilot scheme to promote young researchers

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No