

# Brain imaging of the adenosine A2A receptor in schizophrenia

<b>Submission date</b> 03/02/2014	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 10/02/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 15/05/2018	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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

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## Contact information

### Type(s)

Scientific

### Contact name

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### Contact details

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## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

## **Study design**

Open labelled non-randomized study

## **Primary study design**

Interventional

## **Secondary study design**

Non randomised study

## **Study setting(s)**

Hospital

## **Study type(s)**

Diagnostic

## **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**

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 measure**

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.

**Secondary outcome measures**

No secondary outcome measures

**Overall study start date**

01/04/2014

**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  $\geq 4$ ) 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  $\geq 4$ ) 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

**Age group**

Adult

**Sex**

Male

**Target number of participants**

Healthy volunteers: Up to 6; Schizophrenia patients: 6 medicated and 6 un-medicated

**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**

England

United Kingdom

### **Study participating centre**

**King's College London**

London

United Kingdom

SE5 8AF

## **Sponsor information**

### **Organisation**

King's College London (UK)

### **Sponsor details**

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### **Sponsor type**

University/education

### **ROR**

<https://ror.org/0220mzb33>

## **Funder(s)**

### **Funder type**

University/education

### **Funder Name**

King's College London

**Alternative Name(s)**

Collegium Regale Londiniense, King's, 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

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No