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Neuroimaging effects of a single dose of modafinil on brain activation in patients with schizophrenia

Submission date
08/11/2013

Recruitment status
No longer recruiting

Registration date
08/11/2013

Overall study status
Completed

Last Edited
10/08/2018

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
Cognitive problems, problems with memory, attention and planning, are almost universal in patients with schizophrenia and account for 20-60% of the difference in functional outcome. Cognitive impairment associated with schizophrenia (CIAS) is well established by the time of the first occurrence. Treatment with antipsychotic medications is not effective for CIAS. Some cognitive-enhancing drugs have shown promising results. Current research indicates that cognitive problems in schizophrenia is due to abnormal brain development and disconnections between brain areas. Therefore, it is important to develop new treatment methods to enhance cognition in schizophrenia. Current evidence suggests starting treatment early in the course of schizophrenia is associated with a greater treatment response and longer duration of illness may be associated with more severe brain changes. To understand how cognition-enhancing drugs modify abnormalities in brain networks functioning we will find out the effects of modafinil on both behavioural tests and cognition-related brain networks in volunteers with schizophrenia. Modafinil is the only drug with cognitive-enhancing properties that has been tested in both chronic and recent onset patients and has shown beneficial effects, but how modafinil affects cognition is still unclear.

Who can participate?
People who have experienced non-affective psychosis for the first time in the past three years and is aged 18-35 can participate in the study.

What does the study involve?
Participants will be required to attend four separate appointments. At the first visit (screening), a persons eligibility is assessed and will include taking informed consent, demographics, medical and treatment history, a brief physical examination including an electrocardiogram (ECG), vital signs, urine pregnancy test (if applicable) and some questionnaires. This visit will last approximately 3 hours. In Visit 2, participants will undergo two batteries of neuropsychological tests called MATRICS (pen and paper) and CANTAB (computerised) which assess cognitive functions such as memory, attention, ability for planning, and verbal fluency. Participants will also complete two novel tasks which assess attention and memory. Patients will be randomly

allocated to the study medication order (either modafinil or placebo first) and will be given their first capsule to take home with them which will be taken two hours before visit 3. This visit will last approximately 3 hours.
Visits 3 and 4 are identical. Participants will have taken the study medication two hours prior to the start of the visit. Vital signs will be examined and they will be asked for any drug related side effects. Participants will undergo a one hour magnetic resonance imaging (MRI) scan. During the scan they will perform three tasks measuring working memory and attention, as well as a resting state scan where participants will be asked to remain still with their eyes open. Following the MRI scan, participants will complete the MATRICS and CANTAB neuropsychological batteries. Participants will be given their second capsule at the end of visit 3, which will be taken two hours before visit 4. These visits will last approximately 3.5 hours each and will take place 7-10 days apart. After the completion of visit 4, participants will be followed up for one week. A trained researcher will call once, 5-7 days after visit 4. Participants will be able to call the study mobile telephone 24hrs a day, 7 days a week for the duration of the study.

What are the possible benefits and risks of participating?
This is a research study whose results will be very helpful in gaining a better understanding on the effects of modafinil on psychological abilities of patients with psychosis. Other patients in the future might benefit from the results of the study. However, a single dose of the drug will not be of substantial benefit. The most common side effects are headache, nausea, nervousness, runny nose, diarrhoea, back pain, anxiety, insomnia, dizziness and indigestion. Other reported, but less frequent, unwanted effects include dry mouth, appetite changes, and abdominal pain, rapid heart rate, dilation of blood vessels, chest pain, irregular heartbeat, anxiety, depression, confusion, tingling sensation, lack of energy, rush and visual disturbances. We will monitor all research participants every day during drug intake regarding any side effects they might experience. In addition, all research participants will have a 24 hour contact number of a study doctor. There are no risks from having a magnetic resonance imaging scan. Some people feel uncomfortable in the scanner as space is limited. Participants will be given a button to press if they start to feel uncomfortable during the scan.

Where is the study run from?
The study is being run from the University of Manchester, UK and the Institute of Psychiatry, London, UK.

When is the study starting and how long is it expected to run for?
The study started at the end of October 2013 and is expected to run until 31 August 2014.

Who is funding the study?
Newmeds, an international consortium of scientists, UK.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
15391

Study information

Scientific Title
Neuroimaging effects of a single dose of modafinil on brain activation in patients with schizophrenia: a randomised controlled trial

Study objectives
1. To compare brain activity induced by a single dose of modafinil compared with placebo on the networks involved in attention, working memory and executive function tasks.
2. To study performance of novel neuroscience-based cognitive measures, and compare them to existing measures in terms of sensitivity to the effects of modafinil on CIAS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West Greater Manchester South, 23/09/2013, ref: 13/NW/0626

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)

GP practice

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Topic: Mental Health Research Network; Subtopic: Schizophrenia; Disease: Schizophrenia

Interventions
1. Modafinil. Participants will receive 200mg modafinil on one occasion
2. Placebo: Capsules will be identical to the modafinil capsules, and will contain Lactose

Magnetic resonance imaging (MRI) scans will be carried out by trained radiographers
Follow Up Length: 0 month(s); Study Entry : Single Randomisation only

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Brain activation; Timepoint(s): Mean activation during modafinil compared to placebo during cognitive tasks

Secondary outcome measures
Task Performance; Timepoint(s): Performance on tasks during modafinil compared to placebo

Overall study start date
01/03/2013

Completion date
31/01/2015

Eligibility

Key inclusion criteria
1. Age 18 and 35 years
2. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnosis of schizophrenia, schizophreniform or schizoaffective disorder confirmed by Mini International Neuropsychiatric Interview (MINI)
3. Duration of illness between 1 month and 3 years
4. Patients should be clinically stable in a non-acute phase2 for at least 8 weeks prior to the screening visit
5. Positive and Negative Syndrome Scale (PANSS) Conceptual Disorganization item score = 4
6. PANSS Hallucinatory Behaviour or Unusual Thought Content item scores = 4

7. PANSS Negative Subscale scores on all items = 4
8. Treatment with stable doses of atypical or typical antipsychotics in the absence of concomitant anticholinergics for at least 4 weeks prior to the screening visit
9. Normal baseline electrocardiogram (ECG) prior to randomisation
10. Raw score of 6 or greater on the Wechsler Test of Adult Reading (WTAR)
11. Negative result in urine pregnancy test performed during the screening visit in women of childbearing potential (not surgically sterile or 2 years postmenopausal)
12. Women of childbearing potential, who are sexually active, will be considered as potential participants if they are using acceptable methods of contraception, which include barrier method with spermicide, intrauterine device (IUD), steroidal contraceptive (oral, transdermal, implanted, and injected). Women on combined and progestogen-only contraceptives and on contraceptive patches and vaginal rings will be required to use additional contraceptive precautions for the duration of the trial and 4 weeks after stopping taking modafinil for the study purposes because modafinil may reduce the effectiveness of both combined and progestogen-only contraceptives
12. Subjects must read and write in English at a level sufficient to understand and complete study-related procedures and have legal capacity to consent
13. Written and witnessed informed consent
Target Gender: Male & Female; Upper Age Limit 35 years ; Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 33; UK Sample Size: 33

Key exclusion criteria
1. DSM-IV diagnosis of alcohol or substance abuse (other than nicotine) within the last month or a DSM-IV diagnosis of alcohol or substance dependence (other than nicotine) in the last 6 months preceding the screening visit
2. Treatment with clozapine or thioridazine.
3. Treatment with modafinil
4. Current treatment (within 4 weeks) with psychotropic agents known to affect cognition: amphetamines, barbiturates, lithium, MAOIs, methylphenidate, benzodiazepines, anticholinergics
5. Current treatment (within 4 weeks) with cyclosporine (modafinil reduces plasma concentration of cyclosporine), phenytoin (modafinil possibly increases plasma concentration of phenytoin), anticoagulants (modafinil increases the levels of anticoagulants), tricyclic antidepressants (modafinil may increase their levels)
6. Evidence of tardive dyskinesia, tardive dystonia or other severe chronic movement disorders on physical examination
7. History of neuroleptic malignant syndrome
8. Pregnant or breast-feeding women

9. Clinically significant abnormalities on physical examination
10. History of a serious neurological disorder or a systemic illness with known neurological complications
11. Hypertension, arrhythmia, left ventricular hypertrophy, cor pulmonale, or clinically significant signs of CNS stimulant-induced mitral valve prolapse (including ischemic ECG changes, chest pain and arrhythmias), which pose a risk to the patient if they were to participate in the study
12. Any known drug allergies, including sensitivity to modafinil, and the development of drug-associated rash in the past
13. Prior participation in a study of any psychotropic medication or with a neuopsychological component in the last two months preceding the screening visit
14. Unwillingness or inability to follow or comply with the procedures outlined in the protocol
15. Due to the use of the strong magnet, MRI cannot be performed on patients with implanted pacemakers, intracranial aneurysm clips, cochlear implants, certain prosthetic devices, implanted drug infusion pumps, neurostimulators, bone-growth stimulators, certain intrauterine contraceptive devices, or any other type of iron-based metal implants
16. Presence of internal metallic objects such as bullets or shrapnel, as well as surgical clips, pins, plates, screws, metal sutures, or wire mesh
17. Claustrophobia

Date of first enrolment
28/10/2013

Date of final enrolment
31/08/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Jean MacFarlane Building
University of Manchester
Oxford Rd
Manchester
United Kingdom
M13 9PL

Study participating centre
Institute of Psychiatry, Psychology & Neuroscience
King’s College London
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Sponsor information

Organisation
University of Manchester (UK)

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Sponsor type
University/education

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Government

Funder Name
EU Innovative Medicines Initiative; Grant Codes: 115008

Results and Publications

Publication and dissemination plan
A manuscript covering results from the study have been submitted to a high-impact peer reviewed journal and will be published in late 2017.

Intention to publish date
31/12/2017

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2017		Yes	No
HRA research summary			28/06/2023	No	No