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Neuroimaging the effects of modafinil in healthy volunteers

Submission date
23/04/2014

Recruitment status
No longer recruiting

Registration date
10/06/2014

Overall study status
Completed

Last Edited
10/08/2018

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Problems with memory, attention and planning (cognitive problems) are found in almost all patients with schizophrenia. Cognitive impairment associated with schizophrenia (CIAS) is well established by the time of the first episode but treatment with antipsychotic medications is not effective for CIAS. Some cognitive-enhancing drugs have shown promising results for CIAS where they generally tend to improve individual domains without a clear effect on overall mental ability. The basis of cognitive problems in schizophrenia remains unclear, but current theories link it to abnormal brain development and disconnections between brain areas. To better understand how cognition-enhancing agents work in schizophrenia, it is important to find out how these agents modify task performance and cognition-related brain networks in healthy participants. Modafinil is the only drug with cognitive-enhancing properties that has been tested in both long-term and recent onset patients in single-dose studies and has shown beneficial effects, but how modafinil affects cognition is still unclear. Evidence from functional neuroimaging studies in healthy individuals suggests modafinil improves brain effectiveness during cognitive information processing.

Who can participate?
People with no history of a psychiatric illness or depression, aged 18-35 can participate.

What does the study involve?
Participants will be required to attend four separate appointments. At visit 1, a persons eligibility is assessed and will include taking informed consent, 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 about 3 hours. At visit 2, participants will undergo two sets of tests called MATRICS (pen and paper) and CANTAB (computerised), which assess mental functions such as memory, attention, ability for planning, and verbal fluency. Participants will also complete two tasks which assess attention and memory. Patients will be randomly allocated to receive either a modafinil capsule or a placebo (dummy) capsule first (they will receive the other capsule later) and will be given their first capsule to take home with them, which will be taken 2 hours before visit 3. This visit will last about 3 hours. Visits 3 and 4 are identical. Participants will have taken the study medication 2 hours before the visit. Vital signs will be examined and they will be asked about any drug-related side effects.

Participants will undergo a 1-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 tests. They 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 about 4.5 hours each and will take place 7-10 days apart. After the completion of visit 4, participants will be followed up for 1 week. A trained researcher will call once, 5-7 days after visit 4. Participants will be able to call the study mobile telephone 24 hours a day, 7 days a week for the duration of the study.

What are the possible benefits and risks of participating?
The results of this study will help us gain a better understanding of the effects of modafinil on psychological abilities. The most common side effects are headache, nausea, nervousness, runny nose, diarrhoea, back pain, anxiety, sleeplessness, 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 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 MRI 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 University of Manchester (UK).

When is the study starting and how long is it expected to run for?
June 2014 to February 2015.

Who is funding the study?
Newmeds - EU Innovative Medicines Initiative.

Who is the main contact?
Dr Jane Lees
jane.lees@manchester.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Shon Lewis

Contact details
3rd Floor, Jean McFarlane Building
University of Manchester
Manchester
United Kingdom
M13 9PL

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Neuroimaging effects of a single dose of modafinil on brain activation in healthy volunteers

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 compare brain activity induced by a single dose of modafinil in healthy volunteers to that in patients with schizophrenia

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West Liverpool East, 15/05/2014; ref. 14/NW/0299

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

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
Schizophrenia

Interventions
1. Modafinil: participants will receive 200 mg 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: 5-7 days

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Brain activation: Mean activation during modafinil compared to placebo during cognitive tasks. Measured baseline, follow-up 1 (approx. 1 week after baseline), and follow-up 2 (7-10 days after follow-up 1)

Secondary outcome measures
Task performance: performance on tasks during modafinil compared to placebo. Measured at baseline, follow-up 1 (approx. 1 week after baseline), and follow-up 2 (7-10 days after follow-up 1)

Overall study start date
06/06/2014

Completion date
28/02/2015

Eligibility

Key inclusion criteria
1. Age 18 to 35 years, matched by 5 year bands to previously recruited patient group
2. Gender: Males and Females matched to previously recruited patient group
3. No current or past DSM-IV diagnosis confirmed by Mini International Neuropsychiatric Interview (MINI)
4. No neurological disease (ICD10)
5. Normal baseline electrocardiogram (ECG) prior to randomisation
6. Raw score of 6 or greater on the Wechsler Test of Adult Reading (WTAR)
7. No medications except simple analgesics and contraceptives
8. Negative result in the urine pregnancy test performed during the screening visit in women of childbearing potential (not surgically sterile or 2 years postmenopausal)
9. 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
10. Subjects must read and write in English at a level sufficient to understand and complete study-related procedures
11. Written and witnessed informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
34

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 breastfeeding 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 neuropsychological component in the last 2 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
10/06/2014

Date of final enrolment
27/01/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Manchester
3rd Floor
Jean McFarlane Building
Oxford Road
Manchester
United Kingdom
M13 9PL

Sponsor information

Organisation
University of Manchester (UK)

Sponsor details
FMHS Research Office
3.53 Simon Building
Manchester
England
United Kingdom
M13 9PL

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 has been submitted to a high-impact peer reviewed journal and will be published in 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
Other

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