

# Neuroimaging the effects of modafinil in healthy volunteers

<b>Submission date</b> 23/04/2014	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 10/06/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/08/2018	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> 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

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## Contact information

### Type(s)

Scientific

### Contact name

Prof Shon Lewis

### Contact details

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# Additional identifiers

## Protocol serial number

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

## Study type(s)

Diagnostic

## 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(s)

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)

### **Key secondary outcome(s)**

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)

### **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

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **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**

United Kingdom

England

**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)

### ROR

<https://ror.org/027m9bs27>

## Funder(s)

### Funder type

Government

### Funder Name

EU Innovative Medicines Initiative; Grant Codes: 115008

## Results and Publications

### 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?
<a href="#">Results article</a>	results	01/10/2017		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No