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A pilot study of cognitive enhancer and cognitive training combination: testing a therapeutic paradigm for cognitive impairment in schizophrenia

Submission date
16/07/2010

Recruitment status
No longer recruiting

Registration date
01/10/2010

Overall study status
Completed

Last Edited
20/05/2019

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
Schizophrenia is one of the most disabling psychiatric illnesses: it begins in adolescence and inflicts distress and disability for patient and family, while costing the UK more than £10 billion in lost income and support. Even with the best treatments, only 15% of patients with schizophrenia find paid employment. A major cause of disability are the cognitive symptoms of schizophrenia, i.e. problems in memory, attention, concentration, planning ahead and managing social interactions, also called cognitive impairments. The current treatment for schizophrenia, the antipsychotic medications, helps with the psychotic symptoms (i.e. with the hallucinations and the paranoia) but is not effective for the treatment of cognitive symptoms.
The focus of our study is to improve these cognitive symptoms with the hope that this would allow patients with schizophrenia to increase their everyday functioning. To improve these cognitive symptoms, several medications have been tried in clinical studies without impressive results so far. Cognitive remediation various types of brain training and learning exercises - has also been tried with modest success. In this study we will combine medication with cognitive training exercises to study if their effects on cognitive symptoms of patients with schizophrenia can be boosted.

Who can participate?
Forty patients with schizophrenia in a stable clinical condition will be recruited.

What does the study involve?
Participants will be randomly allocated to receive either modafinil (the cognition enhancing agent) or an inactive compound (dummy drug) and will undergo cognitive training sessions, during which they will complete attention, memory and learning exercises.

What are the possible benefits and risks of participating?
We expect that the combination of modafinil with cognitive training will enhance the cognitive performance of patients and will last after the end of the training and modafinil. Other patients

in the future might benefit from the results of this study, if we are able to establish a new treatment on the basis of this study. Apart from this, we cannot and do not promise that study participants will receive any benefits from this study.
All medicines may cause unwanted side effects, but many people have only minor side effects or none at all. Evidence shows that modafinil is a well-tolerated medication with short-lasting side effects. The most common side effects of modafinil are: headache; nausea; nervousness; diarrhoea, back pain, stomach upset; stuffy nose; trouble sleeping. A medically qualified researcher will monitor study participants on a daily basis for the duration of the study.

Where is the study run from?
It will be conducted in 2 study sites: the Institute of Psychiatry, Kings College London and University of Manchester.

When is the study starting and how long is it expected to run for?
The study will start in late 2010 and is expected to last approximately 2.5 years.

Who is funding the study?
The study is funded by a European Union grant (NEWMEDS).

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2009-013020-23

Protocol serial number
RAA09-002

Study information

Scientific Title

A pilot, randomised placebo-controlled study of cognitive enhancer and cognitive training combination: testing a therapeutic paradigm for cognitive impairment in schizophrenia

Acronym
ModCTCoS

Study objectives
This research focuses on the development of a therapeutic paradigm for the cognitive deficits associated with schizophrenia. Cognitive deficits contribute significantly to functional outcomes of patients with schizophrenia, such as occupational status, social dysfunction and impairment in independent living. Strategies to improve cognition in schizophrenia include pharmacological approaches (based on modulation of brain chemistry), and non-pharmacological approaches (based on training interventions to improve cognitive abilities) - research has shown that the effects of these approaches are modest. A limited number of studies have attempted to combine a cognitive enhancing medication with cognitive training in healthy volunteers and patients with anxiety disorders and Alzheimers disease, with encouraging findings, suggesting that patients who receive combined pharmacological and cognitive training treatment show greater improvement compared to patients who received pharmacological treatment alone. The current research aims to increase the efficacy of these approaches by combining a cognitive enhancing medication with cognitive training in patients with schizophrenia. Thus, the study is a Proof of Principle trial to demonstrate that combining cognitive enhancers with cognitive remediation will have a cumulative learning and/or synergistic effect. Furthermore, combining cognitive enhancers and cognitive training may lead to the development of more economical and efficient designs for medium sized clinical trials.

A secondary aim if the study is examining the validity and reliability of the cognitive outcome measures. The MCCB (MATRICS Consensus Cognitive Battery) is currently considered the gold standard outcome measure in clinical trials of cognition in schizophrenia. However, the MCCB has constraints: as a paper and pencil test the administration is not as reliable as computer based tests i.e. it is subject to the variability of the researchers administering the task. The MCCB is also constrained by largely comprising language based tests. Since the introduction of the MCCB, a computerised Cognitive battery (CogState) has been developed as an alternative. CogState has advantages in utility since it is computerised, and consists of predominantly nonverbal tasks. A secondary interest of the current study is to assess the cross validity of MCCB and CogState, ensuring that both tasks measure the same types of cognitive function.

The main objectives are:
1. To pilot the approach of combining a cognitive-enhancement drug (Modafinil) with cognitive training in patients with schizophrenia
2. To obtain proof-of-concept evidence for the direction of effect and develop the first estimates of effect sizes that can guide future developments

Secondary objectives:
1. To examine the reliability of CogState Schizophrenia Battery and Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Battery (MCCB) in the face of repeated testing
2. To examine the sensitivity of CogState and MCCB to a single dose of Modafinil in patients with schizophrenia

As of 21/02/2012, anticipated end date of trial was updated from 30/04/2011 to 01/12/2012.

Please note that as of 01/03/2013, the anticipated end date for this trial was updated from 01/12/2012 to 29/10/2012

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Charing Cross Research Ethics Committee (REC) approved on the 23rd March 2010 (ref: 10/H0711/14)
2. Medicines and Healthcare Products Regulatory Agency (MHRA) approved (ref: 21416/0220/001-0002)

Study design
Multicentre pilot randomised placebo controlled parallel group trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
The study is a randomised control trial. Participants will be randomised to receive a cognitive enhancer (modafinil) or placebo. Study participants will receive 200mg of modafinil once/day for 12 days. The 1st day of modafinil/placebo treatment, we will assess the effects of a single dose of modafinil on the participants' neuropsychological performance. From day 2 to day 11, all participants will undergo cognitive training exercises after having received the daily dose of modafinil/placebo. On day 12 we will assess the effects of modafinil/placebo+ cognitive training combination on neuropsychological performance.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
The effect of the combination of modafinil and cognitive training on learning capacity of the research participants, i.e. the percentage of correct responses and mean response time on the cognitive training tasks as a function of cognitive training, and the effect of the cobmination of modafinil and training on the cognitive outcome measures (MATRICS Consensus Cognitive Battery [MCCB] and CogState)
Outcomes will be measured every day during the combined intervention period (Day 2 to Day 11) and also once during the 2nd week of the follow-up period.

Key secondary outcome(s))

1. Change in the composite scores of the neuropsychological batteries (CogState and MCCB) scores following a single dose of modafinil
2. Reliabillity of CogState and MACCB batteries in the face of repeating testing

Completion date
29/10/2012

Eligibility

Key inclusion criteria
1. Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) diagnosis of schizophrenia or schizoaffective disorder confirmed by Mini International Neuropsychiatric Interview (MINI)
2. Age between 18 and 50 years
3. Males and females
4. Duration of illness equal to or greater than one year
5. Patients should be clinically stable in a non-acute phase for at least 8 weeks prior to the screening visit
6. Subjects will meet the following symptom criteria
6.1. Positive and Negative Syndrome Scale (PANSS) Conceptual Disorganization item score less than or equal to 4
6.2. PANSS Hallucinatory Behaviour or Unusual Thought Content item scores less than or equal to 4
6.3. PANSS Negative Subscale scores on all items less than or equal to 4
7. Subjects will meet the following cognitive performance criteria
7.1. Raw score of 6 or greater on the Wechsler Test of Adult Reading (WTAR)
8. Treatment with stable doses of atypical antipsychotics for at least 4 weeks prior to the screening visit
9. Negative result in the urine pregnancy test performed during the screening visit in women of childbearing potential (not surgically sterile or 2 years postmenopausal)
10.Women of child-bearing 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.
11. Subjects must read and write in English at a level sufficient to understand and complete study-related procedures
12. Written and witnessed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
49

Key exclusion criteria
1. Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (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
3. Treatment with modafinil
4. Current treatment (within 4 weeks) with psychotropic agents known to affect cognition: amphetamines, barbiturates, lithium, Monoamine Oxidase Inhibitors (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. Pregnant or breast-feeding women
7. Clinically significant abnormalities on physical examination
8. History of a serious neurological disorder or a systemic illness with known neurological complications
9. Hypertension, arrhythmia, left ventricular hypertrophy, cor pulmonale, or clinically significant signs of central nervous system (CNS) stimulant-induced mitral valve prolapse (including ischaemic electrocardiogram [ECG] changes, chest pain and arrhythmias), which pose a risk to the patient if they were to participate in the study
10. Any known drug allergies, including sensitivity to modafinil, and the development of drug-associated rash in the past
11. Unwillingness or inability to follow or comply with the procedures outlined in the protocol
12. Prior participation in a clinical trial of any psychotropic medication in the last 2 months preceding the screening visit

Date of first enrolment
03/04/2010

Date of final enrolment
29/10/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Institute of Psychiatry
London
United Kingdom
SE5 8AF

Sponsor information

Organisation
King's College London (KCL) (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
Innovative Medicines Intiative (IMI) & European Seventh Framework Program (FP7) (Europe) - (ref: IMI_Call2008_1)

Results and Publications

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?
Basic results			20/05/2019	No	No
HRA research summary			28/06/2023	No	No