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Brain stimulation combined with cognitive training in attention deficit hyperactivity disorder

Submission date
09/12/2016

Recruitment status
No longer recruiting

Registration date
31/12/2016

Overall study status
Completed

Last Edited
07/07/2021

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
Around one in 40 children in the UK have attention deficit hyperactivity disorder (ADHD). Children with ADHD tend to be hyperactive and impulsive, and have a short attention span, meaning they are easily distracted. They can't control this behaviour very well, which can seriously impact life at home and at school. This study is investigating the potential of a new, drug-free approach to treatment, which combines a specially designed brain-training video game with electrical brain stimulation. The need for a new treatment that offers long-term benefits for children with ADHD without causing side effects is high. There's no cure for ADHD. Stimulant medication is so far the best working treatment for ADHD, as it improves symptoms in over 70% of patients. However, although medication is often highly effective in the short term, there is little evidence that it helps in the longer term and benefits are immediately lost if children stop taking their medication. What's more, medication can have side effects, it doesn't work for everyone, it is disliked by many teenagers and the long-term effects on the developing brain are unknown. Safer and more effective drug-free treatments would be highly desirable. This study is investigating whether a possible new, drug-free approach to treatment might benefit children with ADHD.

Who can participate?
Boys aged 10-18 with ADHD

What does the study involve?
The treatment involves playing a specially designed video game while receiving what's called transcranial direct current stimulation (tDCS). The video game is designed to help children to become less impulsive and more able to pay attention without being distracted. tDCS involves stimulating underactive areas of the brain with weak electric currents – using electrodes placed on the scalp – and the researchers are investigating whether it enhances the effects of the video game with a group of ADHD boys. The study involves the patient being trained every day for 3 weeks for 20 minutes on a computer game that trains his attention and is aimed to make the child less impulsive. At the same time that the child plays on the computer game, he receives a stimulation of the right frontal part of his brain via tDCS. tDCS is considered safe, does not hurt

and has no side effects (expect for mild transient tingling in some people). The stimulation of the right frontal part of the brain is thought to help the child to activate these regions and this is thought to improve the ability to concentrate and to make him less impulsive. The children are randomly allocated to receive either real stimulation or fake stimulation. Before and after the treatment, the parents have to fill in questionnaires about the behaviour of their child so the study can test whether the child improves in his ADHD behaviours after the 3 week treatment. In addition the child is tested to see whether he becomes better in typical tests of attention, concentration and impulsiveness. The parents also have to fill in some questionnaires 6 months after the treatment, to test whether the effect of the treatment stays after 6 months.

What are the possible benefits and risks of participating in the research?
It is not known whether the treatment will make ADHD children better. Some studies have shown that children with ADHD can become better when they are trained in these specific computer games that are aimed at improving their inattention and impulsivity. What's more, some studies have shown that children with ADHD improve even more in their attention and become less impulsive when they receive brain stimulation together with the video-game. It is thought that children will improve with the treatment but this cannot be guaranteed. Participating in the study therefore may or may not improve ADHD behaviours. Participation in the study will help with the development of a new potentially effective drug-free treatment for ADHD. tDCS is a painless procedure. There are no known risks or side effects of tDCS. The physical sensations are mild, and many participants report being unaware of the stimulation. Some participants report a slightly tingling sensation, and on occasion, participants may report mild local discomfort at the electrode sites, which fades quite quickly as the scalp adapts to the sensations.

Where is the study run from?
King's College London (UK)

When is the study starting and how long is it expected to run for?
November 2017 to March 2021

Who is funding the study?
Action Medical Research (UK)

Who is the main contact?
Prof. Katya Rubia

Contact information

Type(s)
Scientific

Contact name
Prof Katya Rubia

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Additional identifiers

Protocol serial number
1234

Study information

Scientific Title
A novel brain-based therapy for attention deficit hyperactivity disorder children using transcranial direct current stimulation combined with cognitive training

Acronym
ADHDBRAINSTIM

Study objectives
The hypothesis is that direct current brain stimulation over right inferior frontal cortex combined with cognitive training will improve cognitive performance and symptoms of attention deficit hyperactivity disorder (ADHD) children.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Camberwell St Giles Research Ethics Committee, 18/07/2017, REC ref: 17/LO/0983, IRAS project ID: 221680

Primary study design
Interventional

Study design
Double-blind placebo-controlled randomised controlled interventional trial at a single center

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Attention deficit hyperactivity disorder (ADHD)

Interventions
Updated 01/05/2020: current interventions since REC approval 18/07/2017:
Transcranial direct current stimulation (tDCS) (1mA) combined with cognitive training on ADHD-relevant computerised training tasks of attention, inhibition and timing. Patients are randomly allocated to a sham-stimulation or real stimulation, both during cognitive training. The intervention will be administered for 20 min each week-day for 3 weeks.

tDCS and cognitive training: tDCS will be administered using a battery-driven constant-current DC-Stimulator by INNOSPHERE. A single current of 1mA will be applied for 20 minutes (optimal and safe amplitude and time period) by two saline-soaked brush electrodes. The anodal electrode will be placed over right inferior frontal cortex (rIFC), the cathodal electrode over the left eye-brow. Sham tDCS will be identical, but stimulation will be switched off after 60 s. Naïve subjects cannot feel the difference between real and sham tDCS. During tDCS, patients will perform the validated cognitive training games for ADHD, developed by Co-PI Prof Wexler, Yale University, which trains inhibition, sustained attention, processing speed and working memory.

Previous interventions:
Transcranial direct current stimulation (tDCS) (1mA) combined with cognitive training on ADHD-relevant computerised training tasks of attention, inhibition and timing. Patients are randomly allocated to a sham-stimulation or real stimulation, both during cognitive training. The intervention will be administered for 20 min each day for 2 weeks.

tDCS and cognitive training: tDCS will be administered using a battery-driven constant-current DC-Stimulator by NeuroConn. A single current of 1mA will be applied for 20 minutes (optimal and safe amplitude and time period) by two saline-soaked sponge covered electrodes. The anodal electrode will be placed over right inferior frontal cortex (rIFC), the cathodal electrode over the left eye-brow. Sham tDCS will be identical, but stimulation will be switched off after 60 s. Naïve subjects cannot feel the difference between real and sham tDCS. During tDCS, patients will perform the validated CT task for ADHD, developed by Co-PI Prof Wexler, Yale University, which trains inhibition, sustained attention, processing speed and working memory.

At follow-up, the primary outcome measure will be assessed with the parents via telephone 6 months after the intervention.

Intervention Type
Device

Primary outcome(s)
Updated 01/05/2020: current primary outcome measures since ethics approval on 18/07/2017:
Measured immediately before and after the intervention and 6 months after the intervention:
1. Cognitive performance outcome variables, measured using a cognitive task battery developed for ADHD that measures key functions typically impaired in the disorder including motor inhibition (Go-no-go task) and sustained attention (Continuous Performance Task).
2. ADHD symptoms, measured on the ADHD-Rating Scale (ADHD-RS)

Previous primary outcome measures:
Measured immediately before and after the intervention and 6 months after the intervention:
1. Cognitive performance outcome variables, measured using a cognitive task battery developed for ADHD that measures key functions typically impaired in the disorder including motor and interference inhibition, switching, sustained attention, time estimation, and temporal discounting
2. ADHD symptoms, measured on the ADHD-Rating Scale (ADHD-RS)

Key secondary outcome(s)
Updated 01/05/2020: current secondary outcome measures since ethics major amendment 21/11/2017:
Measured immediately before and after the intervention:
1. The ADHD Index of the Conners Parent Rating Scales (CPRS)

2. Other clinical measures:
2.1. The Columbia Impairment Scale (CIS)
2.2. The WREMB-R, Weekly Rating of Evening and Morning Behavior-Revised
2.3. The Affective Reactivity Index (ARI)
2.4. The Mind excessive wandering scale (MEWS)
3. Side effects
4. Other cognitive measures:
4.1. Wisconsin Card Sorting Test (WCST)
4.2. Vigilance task
4.3. Simon Interference inhibition task
4.4. Time estimation task
4.5. Visual-spatial working memory task
4.5. Verbal and semantic fluency task
5. EEG measures at pre and post assessment and follow-up during rest and Go-no-go task (10min)
6. Long-term effects, assessed 6 months after the intervention in the primary outcome measures, in the CPRS, ARI, MEWS and in all cognitive tasks

Previous secondary outcome measures:
Measured immediately before and after the intervention:
1. The ADHD Index of the Conners Parent Rating Scales (CPRS)
2. Other clinical measures:
2.1. Clinical Global Impression ADHD severity scale (CGI)
2.2. The Columbia Impairment Scale (CIS)
2.3. The Child Health Questionnaire
3. Side effects
4. Long-term effects, assessed 6 months after the intervention in the primary outcome measures

Completion date
02/03/2021

Eligibility

Key inclusion criteria
Updated 12/05/2020: current inclusion criteria since ethics approval on 18/07/2017:
1. Age range: 10-18 years
2. Gender: male
3. Meeting DSM-5 diagnosis of ADHD
4. Score above clinical cut-off on the Schedule for Affective Disorders and Schizophrenia, ADHD module (K-SADS)
5. Score about clinical cut-off for ADHD on the short forms of the Conners Parent Rating Scales (CPRS)
6. Patients will be either medication naïve or on their usual stable medication without change in regime throughout the study
7. IQ > 80 as tested on the 4 subtests of the WASI (Wechsler, 1999) that assesses intellectual ability of individuals aged 6 years and over. Administration of 4 subtests takes ~ 40 minutes, and produces a full-scale IQ score

Comorbidity with other disorder will be allowed except the ones outlined below under exclusion criteria

Previous inclusion criteria:
1. Age range: 10-17 years
2. Gender: male
3. Meeting DSM-5 diagnosis of ADHD
4. Score above clinical cut-off on the Schedule for Affective Disorders and Schizophrenia, ADHD module (K-SADS)
5. Score about clinical cut-off for ADHD on the short forms of the Conners Parent and Teacher Rating Scales (CPRS/CTRS)
6. Patients will be either medication naïve or on their usual stable medication without change in regime throughout the study
7. IQ > 80 as tested on the 4 subtests of the WASI (Wechsler, 1999) that assesses intellectual ability of individuals aged 6 years and over. Administration of 4 subtests takes ~ 40 minutes, and produces a full-scale IQ score

Comorbidity with other disorder will be allowed except the ones outlined below under exclusion criteria

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
10 Years

Upper age limit
18 Years

Sex
Male

Total final enrolment
50

Key exclusion criteria
1. IQ < 80
2. Comorbidity with schizophrenia, Bipolar disorder, learning disability, severe depression with current suicidal behaviour (as assessed by clinician)
3. Neurological problems, i.e. a history of severe neurological illness, e.g. brain tumour, epilepsy or a history of symptomatic seizures, polyneuropathy etc
4. Substance abuse history
5. Contraindication to neurostimulation. i.e., previous implantation of metallic material (e.g., vascular clips, cochlear implant) in the cranium (except in the mouth), pacemaker, implanted medication pumps, neural stimulators
6. Drug treatment acting primarily on the central nervous system which lowers the seizure threshold such as antipsychotic drugs (chlorpromazine, clozapine) or tricyclic antidepressants
7. Diseased or damaged skin over the face or scalp

8. History of migraine (brain stimulation may increase susceptibility to headaches in migraineurs)
9. Unable to give informed assent or consent in the case of the primary caregiver

Date of first enrolment
12/02/2018

Date of final enrolment
01/09/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College London
Department of Child & Adolescent Psychiatry/Social Genetic and Developmental Psychiatry Center (SGDP) PO46
Institute of Psychiatry, Psychology & Neurosciences
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United Kingdom
SE5 8AF

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Charity

Funder Name
Action Medical Research

Alternative Name(s)
action medical research for children, actionmedres, The National Fund for Research into Crippling Diseases, AMR

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are available from Prof. Katya Rubia on reasonable request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		06/07/2021	07/07/2021	Yes	No
HRA research summary			28/06/2023	No	No