Experimental fMRI Study of Guanfacine and Lisdexamfetamine in ADHD Adolescents (AGUALIS)

This study is not yet open for participant recruitment. See Contacts and Locations

Verified October 2017 by King's College London

Sponsor:
King's College London

ClinicalTrials.gov Identifier:
NCT03333668

First Posted: November 7, 2017
Last Update Posted: November 7, 2017

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Collaborator:
Shire

Information provided by (Responsible Party):
King's College London

Purpose
This is not a clinical trial. The aim of this study is to understand the mechanism of action of two recently licensed drugs for ADHD on brain function. We will compare the brain activation changes elicited by Guanfacine extended release (GXR; a non-stimulant drug) with the brain activation changes elicited by Lisdexamfetamine (LISDEX; a stimulant drug) and by placebo in 20 drug-naïve patients with ADHD using functional Magnetic Resonance Imaging (fMRI). For this purpose we intend to scan participants during their performance of tasks of attention, working memory, and inhibition, which we know from previous studies to elicit abnormal brain activation patterns in ADHD patients (Rubia et al., 2005; Smith et al., 2006).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
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<tbody>
<tr>
<td>ADHD</td>
<td>Drug: Lisdexamfetamine dimesylate Drug: Guanfacine Extended Release Oral Tablet Drug: Placebo</td>
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</table>

Study Type: Intervventional

Study Design: Allocation: Randomized Intervention Model: Crossover Assignment Intervention Model Description:

Each participant will complete all three experimental conditions (LISDEX, GXR, placebo) in a randomised order.

Masking: Double (Participant, Investigator)
Primary Purpose: Basic Science
Official Title: Experimental fMRI Study on the Comparison of the Brain Function Effects of a Single Dose of Guanfacine and Lisdexamfetamine Relative to Placebo in Children and Adolescents With ADHD.

Resource links provided by NLM:

Drug Information available for: Guanfacine Guanfacine hydrochloride Lisdexamfetamine Lisdexamfetamine dimesylate

U.S. FDA Resources

Further study details as provided by King's College London:

Primary Outcome Measures:
- Change in brain activation under the three drug conditions (LISDEX, GXR, placebo) [Time Frame: 2 weeks (3 hourly scans one week apart)]

Brain activation as measured by blood-oxygen-level-dependent (BOLD) response obtained by fMRI for each of the 3 below listed tasks and functional connectivity measures for the resting state scan.
  1. A working memory task (N-back)
  2. A tracking stop task
  3. A parametric sustained attention task

Secondary Outcome Measures:
- Changes in dependent variables extracted from performance on the fMRI tasks used under the three drug conditions (LISDEX, GXR, placebo) [Time Frame: 2 weeks (3 hourly scans one week apart)]
  1. A working memory task (N-back)
  2. A tracking stop task
  3. A parametric sustained attention task

Estimated Enrollment: 20
Anticipated Study Start Date: March 1, 2018
Estimated Study Completion Date: December 31, 2020
Estimated Primary Completion Date: December 31, 2020 (Final data collection date for primary outcome measure)

<table>
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<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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<tbody>
<tr>
<td>Active Comparator: Lisdexamfetamine - Placebo</td>
<td>Drug: Lisdexamfetamine dimesylate&lt;br&gt;Lisdexamfetamine dimesylate (30mg for smaller, 50mg for larger boys) tablet&lt;br&gt;Other Name: Vyvanse (Shire Pharmaceuticals Ltd.)&lt;br&gt;Drug: Placebo&lt;br&gt;Vitamin C (10mg) tablet</td>
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<tr>
<td>Active Comparator: Guanfacine - Placebo</td>
<td>Drug: Guanfacine Extended Release Oral Tablet&lt;br&gt;Guanfacine Extended Release (0.05mg/kg) tablet&lt;br&gt;Other Name: Intuniv (Shire Pharmaceuticals Ltd.)&lt;br&gt;Drug: Placebo</td>
</tr>
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</table>
Detailed Description:
Twenty ADHD male patients between 10 and 18 years will participate in the double-blind, randomised, active drug condition, within-group, placebo-controlled experimental fMRI study. Each participant will be assessed in baseline measures during a pre-assessment visit. Then the patient will be scanned 3 times under each of these 3 drug conditions: GXR, LISDEX, and placebo. Every patient will receive a single typical clinical weight-adjusted dose of GXR (0.05mg/kg), LISDEX (30mg for smaller, 50mg for larger boys) and placebo (10mg Vit C) in one of the scans, in a randomised order. Patients will be scanned 4.5 hours after drug administration (where drugs have shown to have maximum plasma concentration). They will be scanned 3 times, one week apart, under each drug condition.

Information from the National Library of Medicine
Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study: 10 Years to 18 Years (Child, Adult)
Sexes Eligible for Study: Male
Accepts Healthy Volunteers: No

Criteria
Inclusion Criteria:
- Age range: 10-18 years
- Gender: male
- Medication-naive or on no medication for 2 or more years
- Handedness: right-handed
- Weight: 20-80 kg
- Meeting DSM-5 diagnosis of ADHD
- Score above clinical cut-off on the ADHD module of the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (Kaufman et al., 1997)
- Score below clinical cut-off for ASD on the Social Communication Questionnaire (SCQ) (Rutter et al., 2003)
- Score above clinical cut-off for ADHD on the short forms of the Conners Parent Rating Scales, CPRS (Conners et al., 2008)
- Score above cut-off on the ADHD Rating Scale, ADHD-RS (DuPaul, et al., 1998)
- IQ > 80 as tested on the WASI-II (Wechsler et al., 1999)
- Mood and depression symptoms will be allowed as long as they are not the primary diagnosis.

Exclusion Criteria:
- IQ < 80 (Wechsler et al., 1999).
- Comorbidity with schizophrenia, bipolar disorder, learning disability, autism, OCD, severe depression with current suicidal behaviour (as assessed by a clinical interview)
- Neurological problems, i.e. a history of severe neurological illness, e.g. brain tumour, epilepsy or a history of symptomatic seizures, polyneuropathy etc.
- Substance abuse history
- Other illness (cardiovascular, renal, hepatic, metabolic) that would impact the data integrity or safety of the subject (i.e. contraindicated to any of the treatments) as determined by the investigators
- Contraindication to MRI, i.e., previous implantation of metallic material, pacemaker, implanted medication pumps, neural stimulators, claustrophobia
- Unable to give informed assent or consent in the case of the parent
- Contraindications for LISDEX and GXR use (i.e. advanced arteriosclerosis, agitated states, hyperexcitability, hyperthyroidism, moderate or severe hypertension, symptomatic cardiovascular disease)

Contacts and Locations

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): NCT03333668

Contacts

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Locations

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Sub-Investigator: Katya Rubia, PhD
Sub-Investigator: Mitul A Mehta, PhD

Sponsors and Collaborators
King's College London
Shire

Investigators

Principal Investigator: Olivia S Kowalczyk, BSc  IoPPN, King's College London

More Information

Publications:

Responsible Party: King's College London
ClinicalTrials.gov Identifier: NCT03333668  History of Changes
Other Study ID Numbers: PCCWUAR
First Submitted: October 31, 2017
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Last Verified: October 2017
Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Undecided

Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No
Product Manufactured in and Exported from the U.S.: No

Keywords provided by King's College London:
Lisdexamfetamine
Guanfacine
functional Magnetic Resonance Imaging
Attention Deficit Hyperactivity Disorder

Additional relevant MeSH terms:
Guanfacine
Lisdexamfetamine Dimesylate
Antihypertensive Agents
Adrenergic alpha-2 Receptor Agonists
Adrenergic alpha-Agonists
Adrenergic Agonists
Adrenergic Agents
Neurotransmitter Agents

Molecular Mechanisms of Pharmacological Action
Physiological Effects of Drugs
Central Nervous System Stimulants
Dopamine Uptake Inhibitors
Neurotransmitter Uptake Inhibitors
Membrane Transport Modulators
Dopamine Agents