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What causes high blood pressure in young people: the heart or blood vessels?

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Registration date 09/08/2023	**Overall study status** Ongoing	
Last Edited 09/08/2023	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Around a third of the adult population suffers from high blood pressure (medically known as “hypertension”). If left untreated, hypertension is a major risk factor for having a heart attack or a stroke. More and more children are being diagnosed with high blood pressure with no obvious cause. This is partly because doctors are checking for it more, but also because it is a common problem that develops alongside being overweight. Not much is known about what causes hypertension in children. This research aims to address this gap by looking in detail at a group of hypertensive children and young adults and comparing them to a group with normal blood pressure. The study will use state-of-the-art blood pressure measurements and heart scans to measure the flow of blood in the heart and blood vessels of participants. The study will also manipulate some of the messages getting from the brain to control the heart and blood vessels and measure the effect of these.

Who can participate?
Children and young adults with primary hypertension aged 10 to 35 years old and under the care of specialist teams at St Thomas’ Hospital and Evelina London Children’s Hospital. Children and young adults who are healthy with normal weight and normal blood pressure aged 10 to 35 years old.

What does the study involve?
The study involves having two different types of heart scan: an echocardiogram and an MRI scan, plus some detailed blood pressure measurements including whilst doing a slow breathing exercise for about 15 minutes. The team will also collect blood and urine samples (optional for healthy participants).

What are the possible benefits and risks of participating?
There are no direct benefits to you from taking part. You will be contributing to research that will improve understanding of high blood pressure which may benefit people of all ages with high blood pressure in the future.

There are no serious risks we anticipate in this study. The main drawbacks of taking part are the extra time and inconvenience for you to visit the hospital for the research study and the discomfort you may experience in the MRI scanner and having a blood test.

Where is the study run from?
St Thomas' Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2022 to September 2026

Who is funding the study?
The Medical Research Council (MRC) (UK)

Who is the main contact?
Dr Emily Haseler, emily.haseler@kcl.ac.uk (UK)

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
306122

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 55164, IRAS 306122

Study information

Scientific Title
Haemodynamic determinants of hYpertension in Children and Young People and role of the sympathetic nervous system: HY CYP

Acronym
HY CYP

Study objectives

Primary hypertension in children results predominantly from cardiac overactivity (increased heart rate, cardiac output and aortic ejection velocity) and a secondary increase in proximal aortic stiffening rather than an increase in systemic vascular resistance.
Cardiac overactivity activity in primary hypertension results from increased sympathetic nervous system activity, mediated through β-adrenergic receptors acting to increase heart rate, stroke volume, cardiac output and aortic ejection velocity.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/06/2023, South Birmingham Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ , United Kingdom; None available; Southbirmingham.rec@hra.nhs.uk), ref: 23/WM/0122

Study design
Observational cohort study (study 1) with an interventional substudy (study 2)

Primary study design
Observational

Secondary study design
Observational cohort study (study 1) with an interventional substudy (study 2)

Study setting(s)
Other

Study type(s)
Treatment

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
Paediatrics and cardiology

Interventions
PARTICIPANTS
Children and young adults with primary hypertension aged 10-35 years will be approached by a member of their direct clinical care team. We aim to recruit 50 patients, 50% under 18 years and 50% 18-35 years, with 50% female. Participants should not be on medication (i.e., are managing their hypertension with lifestyle modification measures). If they are on medication, they need to be able to stop their medication for a 2-week washout period before the study and stay off their medication until the collection of all data (up to 2 months), in the opinion of their lead clinician. For Study 2, we will seek to recruit 20 hypertensive patients from the original Study 1 cohort, at the point at which they will be commencing antihypertensive medication for clinical reasons.

50 control participants aged 10-35 years will be recruited from existing databases of healthy controls. These participants have previously participated in clinical studies with our group and have consented to be contacted about further studies in the future. We aim to recruit 50

patients, 50% under 18 years and 50% 18-35 years, with 50% female. They will need to be of normal blood pressure and healthy weight, i.e., not overweight, or obese.

STUDY 1 (all 100 participants)
Data to be collected is as follows, with no specific order necessary:
1. Height, weight, BMI, and measures of adiposity. Pubertal status for those who have not yet completed puberty.
2. Standardised depression and anxiety questionnaire
3. Blood test: kidney function, measures of sympathetic nervous system activity, measures of heart function, metabolic markers
4. Urine test: sodium (salt) levels, measures of sympathetic nervous system activity
5. Cardiac MRI: 40-minute MRI scan of the heart with blood pressure measured before and after the scan
6. Blood pressure, heart rate variability and arterial applanation tonometry measurements: these are non-invasive and require inflation of a blood pressure cuff, placement of electrode (ECG) stickers on the chest and/or limbs and placing a probe over the pulse points in the neck, groin and wrist respectively.
7. Echocardiogram: a 30-minute ultrasound scan of the heart. This is clinically indicated for all hypertensive participants however some more detailed images will be captured for research, lengthening the scan by 10 minutes.
8. Device-guided breathing: participants will be asked to listen to an audio track which helps them slow their breathing. This has the effect of inhibiting the sympathetic nervous system and lowering blood pressure. Limited echocardiogram and haemodynamic measurements as listed in (6) will be performed. This is likely to take 10-20 minutes depending on how long each participant takes to achieve a steady state with their breathing.

We anticipate that all investigations in Study 1 may be completed in two visits, at least one of which could be on the same day as a clinical visit.

STUDY 2 (a subgroup of 20 hypertensive participants):
1. Administration of antihypertensive agent 1 (bisoprolol): participants will take this medication for 10-14 days at a clinically effective dose. A limited echocardiogram and haemodynamic measurements as listed above in (6) will be performed. This visit will take 15-30 minutes.
2. Administration of antihypertensive agent 2 (amlodipine): participants will take this medication for 10-14 days at a clinically effective dose. Echocardiogram and haemodynamic measurements as listed above in (6) will be performed. This visit will take 15-30 minutes. The order in which participants receive antihypertensive agents 1 and 2 will be randomised.

Intervention Type
Mixed

Primary outcome measure
1. Cardiac output measured MRI at baseline in hypertensive participants compared to healthy controls
2. Aortic ejection velocity measured using MRI at baseline in hypertensive participants compared to controls

Secondary outcome measures
1. Cardiac output measured using an echocardiogram before and after i) slow breathing exercise, ii) amlodipine administration and iii) bisoprolol administration
2. Aortic ejection velocity measured using echocardiogram before and after i) slow breathing

exercise, ii) amlodipine administration and iii) bisoprolol administration
3. Pulse wave velocity measured using applanation tonometry before and after i) slow breathing exercise, ii) amlodipine administration and iii) bisoprolol administration
4. Systemic vascular resistance, heart rate, stroke volume and pulse wave velocity measured using MRI at baseline in hypertensive participants compared to controls

Overall study start date
01/03/2022

Completion date
30/09/2026

Eligibility

Key inclusion criteria
1. Aged 10-35 years old
2. Primary hypertension (intervention group) or BP < 90th centile (control group)
3. Able to tolerate the planned investigations
4. Not currently on anti-hypertensive medication/s or able to stop anti-hypertensive medications for 2 weeks prior to any research-related assessments.

Additional inclusion criteria control participants:
5. BMI in the "normal" range for age

Participant type(s)
Patient

Age group
Mixed

Lower age limit
10 Years

Upper age limit
35 Years

Sex
Both

Target number of participants
Planned Sample Size: 100; UK Sample Size: 100

Key exclusion criteria
1. Secondary hypertension
2. Clinical urgency to commence anti-hypertensive or unable to stop anti-antihypertensives for 2 week washout period
3. Unable to obtain adequate quality of planned cardiovascular investigations
4. Congenital heart disease
5. Cardiac dysrhythmias
6. Pregnancy or lactating mothers

Additional exclusion criteria for medication 1 (bisoprolol challenge):
7. Asthma currently treated with medication
8. Cardiac conduction abnormalities
9. Known intolerance to bisoprolol

Additional exclusion criteria for medication 2 (amlodipine challenge):
10. History of angina or myocardial infarction
11. Known intolerance to amlodipine

Date of first enrolment
01/09/2023

Date of final enrolment
31/08/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Thomas' Hospital
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Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
30/09/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Manish Sinha, manish.sinha@gstt.nhs.uk. These datasets include haemodynamic baseline data from echocardiograms and cardiac MRI, available from approximately September 2027, patients will be consented for sharing of anonymised data.

IPD sharing plan summary
Available on request