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Fatigue In Subclinical Hypothyroidism

Submission date	Recruitment status	[ ] Prospectively registered
06/01/2010	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
15/05/2013	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
22/02/2019	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Having a mild underactive thyroid (thyroid gland not producing enough hormone) is a common medical condition affecting 5-10% of the general population. Fatigue and problems relating to ones thought process (cognitive symptoms) are frequently reported in patients with this condition. It is unclear whether these symptoms are caused by the underactive thyroid. The study aims to find out the mechanisms of fatigue and cognitive symptoms in patients with this condition.

Who can participate?
We aim to recruit 20 patients with mild thyroid underactive state (men or women, aged between 18 and 65 years) and 20 healthy volunteers who will act as control.

What does the study involve?
Patients and healthy volunteers will undergo preliminary clinical assessment. If they are eligible, then they will have a series of tests. These involve magnetic resonance imaging scans (MRI scans) of the brain, heart and leg muscle; assessing heart rate and blood pressure over a period of 2 hours; and psychometric tests for intelligence, reading and memory. The patients will have these tests again after being given thyroxine treatment for 6 months.

What are the possible benefits and risks of participating?
Participants may or may not benefit personally by taking part in this study. But the results may eventually change how we manage fatigue in the future and therefore have benefits for others. The study involves a series of assessments, which means we will be asking for a significant amount of time. Furthermore, there is a very small possibility that during the tests we may discover an incidental abnormality that we have not expected. If this is the case we will liaise with the participants doctor in order to ensure that any appropriate action is taken. Patients may experience mild side-effects from thyroxine treatment if they take too much, but this is monitored closely.

Where is the study run from?
The study has been set up by Gateshead Health NHS Trust, Gateshead, UK.

When is the study starting and how long is it expected to run for?
January 2010 to January 2012

Who is funding the study?
BUPA Foundation (UK)

Who is the main contact?
Prof Julia Newton
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Contact information

Type(s)
Scientific

Contact name
Prof Julia Newton

Contact details
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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Investigating the mechanisms of muscle fatigue and cognitive symptoms in subclinical hypothyroidism

Acronym
FISH

Study objectives
Individuals with subclinical hypothyroidism (SCH) have fatigue due to a combination of cerebral, cardiac and skeletal muscle abnormalities as well as autonomic dysfunction and that this fatigue is (partly or fully) reversible with treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Newcastle & North Tyneside 2 Research Ethics Committee approved on the 20/08/2009, ref: NO-08/H0907/53

Study design
Single centre open label trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Subclinical hypothyroidism

Interventions
All patients are treated with tablet thyroxine for 6 months, at a dose of 1.6 µg/Kg, titrated 6 - 8 weekly, to attain a TSH of 1 - 1.5 mU/L.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Thyroxine

Primary outcome(s)
1. Brain magnetic resonance imaging (MRI) - regional cerebral blood flow and activation of specific regions of intererest during N-back testing at baseline and 6 months
2. Muscle MRI - during rest, exercise and recovery-muscle pH, pH recovery, phosphocreatinine and recovery, inorganic phosphate/adenosine tri-phosphate (ATP) ratio at baseline and 6 months
3. Cardiac MRI - phosphocreatinine/ATP ratio at rest at baseline and 6 months
4. Autonomic function tests at baseline and 6 months:
4.1. Active standing for 3 minutes
4.2. Valsalva's manoeuver
4.3. Tilt testing - 40 minutes
4.4. Heart rate variability (HRV) - time and frequency domain analysis during rest, during and recovery from above manoeuvers
5. Psychometric questionnaires at baseline and 6 months:
5.1. Wechsler Abbreviated Scale of Intelligence (WASI)
5.2. Wechsler Test of Adult Reading (WTAR)
5.3. The Controlled Oral Word Association Test
5.4. Wechsler Memory Scale-III abbreviated (WMS)
6. Fatigue Impact Symptom Score at baseline and 6 months
7. Thyroid Symptom Check List and quality of life questionnaires at baseline and 6 months

Key secondary outcome(s))
No secondary outcome measures

Completion date
10/01/2012

Eligibility

Key inclusion criteria
1. Aged 18 to 65 years
2. Subjects with confirmed SCH thyroid stimulating hormone (TSH) between 4.1 and 10.0 for more than 3 months
3. Fatigue Impact Score greater than 40

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Subjects with previous thyroid disease or on thyroid hormone replacement, anti-thyroid drugs, oral contraceptive pill (OCP), hypotensive agents, aspirin, statins or angiotensin converting enzyme (ACE) inhibitors/angiotensin receptor blocker
2. Subjects with known diabetes mellitus/impaired glucose tolerance (IGT)/impaired fasting glucose (IFG)
3. Known renal failure or a serum creatinine greater than 120 µmol/l within the past 3 months
4. Previous participation in a clinical trial within the past month
5. Previous history of vascular/heart disease
6. Malignancy (any)
7. Active infections
8. Body mass index (BMI) greater than 35
9. Psychiatric disease
10. Drug abuse
11. Previous major head injuries/epilepsy
12. Pacemakers/cerebral aneurysm clips
13. Pregnancy

Date of first enrolment
07/01/2010

Date of final enrolment
10/01/2012

Locations

Countries of recruitment

United Kingdom

England

Study participating centre
FASS unit
Newcastle upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Charity

Funder Name
BUPA Foundation (UK) (ref: 22094167)

Alternative Name(s)

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

IPD sharing plan summary

Not provided at time of registration