

# Fatigue In Subclinical Hypothyroidism

<b>Submission date</b> 06/01/2010	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 15/05/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 22/02/2019	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> 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  
Julia.Newton@ncl.ac.uk

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof Julia Newton

**Contact details**  
FASS unit  
Leazes Wing  
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NE1 4LP

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
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

**Secondary study design**

Non randomised study

**Study setting(s)**

Hospital

**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**

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 measure**

1. Brain magnetic resonance imaging (MRI) - regional cerebral blood flow and activation of specific regions of interest 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 manoeuvre
  - 4.3. Tilt testing - 40 minutes

- 4.4. Heart rate variability (HRV) - time and frequency domain analysis during rest, during and recovery from above manoeuvres
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

### **Secondary outcome measures**

No secondary outcome measures

### **Overall study start date**

07/01/2010

### **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

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

### **Target number of participants**

30

### **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**

England

United Kingdom

**Study participating centre**

**FASS unit**

Newcastle upon Tyne

United Kingdom

NE1 4LP

## **Sponsor information**

**Organisation**

Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

**Sponsor details**

c/o Dr Lesley Hall, PhD

Research and Development Manager

Joint Research Office

4th Floor Leazes Wing

Royal Victoria Infirmary

Queen Victoria Road

Newcastle upon Tyne

England

United Kingdom

NE1 4LP

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.newcastle-hospitals.org.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**

**Publication and dissemination plan**

Not provided at time of registration

2016 results published in thesis <https://theses.ncl.ac.uk/dspace/handle/10443/3242>

**Intention to publish date****Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration