Trial Description

Title

Consequences of short-term hypo- and hyperthyroidism on brain structure and function in humans

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

This project aims to investigate the effects of mild hypo- and hyperthyroidism on higher cognitive function, white and grey brain matter structure, brain functional connectivity and brain perfusion. In addition to the measurement of thyroid function alterations of serum/plasma biomarkers will evaluated using an unsupervised proteomic/metabolomic approach. Mild forms of hypo- und hyperthyroidism will be achieved by reducing thyroxine substitution of patients under full dose of thyroid hormone replacement and by applying thyroxine to healthy volunteers. The planned approach will allow to exactly define thyroxine dependend effects on both cognitive function and peripheral biomarkers in relation to changes in thyroid function.

Brief Summary in Scientific Language

This project will provide a comprehensive picture of the effects of mild hypo- and hyperthyroidism on higher cognitive function, white and grey brain matter structure, brain functional connectivity and brain perfusion, by using state of the art multimodal neuroimaging and neurocognitive testing as well as monitoring of biomarkers. Such a data base is necessary for the understanding of the scope of thyroid hormone action in the CNS. Moreover, using an existing extensively phenotyped (cognitive functions, personality, imaging) cohort, we will assess the effects of genetic differences in thyroid hormone transporters (polymorphisms of MCT8) on the central availability of thyroid hormones indexed by cognitive function and brain structural measures.

Organizational Data

- DRKS-ID: DRKS00011275
- Date of Registration in DRKS: 2016/11/16
- Date of Registration in Partner Registry or other Primary Registry: [---]*
Investigator Sponsored/Initiated Trial (IST/IIT): yes
Ethics Approval/Approval of the Ethics Committee: Approved
(leading) Ethics Committee Nr.: 11-221, Ethik-Kommission Universität zu Lübeck Medizinische Fakultät des Universitätsklinikums Schleswig-Holstein

Secondary IDs

- Universal Trial Number (UTN): U1111-1189-4595

Health condition or Problem studied

- Free text: Effects of mild hyper- and hypothyroidism

Interventions/Observational Groups

- Arm 1: Induction of mild biochemical hyper- or hypothyroidism by application of thyroxine to healthy volunteers or by reduction of the thyroxine dose in patients depending on a full thyroxine substitution

Characteristics

- Study Type: Interventional
- Study Type Non-Interventional: [--]*
- Allocation: Single arm study
- Blinding: [--]*
- Who is blinded: [--]*
- Control: Uncontrolled/Single arm
- Purpose: Basic research/physiological study
- Assignment: Single (group)
- Phase: N/A
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): No

Primary Outcome
Cognitive functions were assessed by resting state and functional MRI under short-term memory challenge. Arterial spin labelling, voxel based morphometry as well as a battery of neuropsychological tests (visual analogue scale for hyper- or hypothyroidism, battery for attention testing, attention network task, trail making task, auditory verbal learning test both during euthyroidism and following 8 weeks of alteration of thyroid function as tested by thyroid function tests in the 2 groups of test subjects will be used.

**Secondary Outcome**

New biomarkers derived from serum and plasma samples in parallel to the samples obtained for thyroid function tests will be used. During the alteration of thyroid function but also in the recovery period up to 8 weeks after we will use an unsupervised approach by the help of proteomics and metabolomics techniques.

**Countries of recruitment**

- DE Germany

**Locations of Recruitment**

- University Medical Center Neurologie, Lübeck

**Recruitment**

- Planned/Actual: Actual
- (Anticipated or Actual) Date of First Enrollment: 2013/03/22
- Target Sample Size: 40
- Monocenter/Multicenter trial: Monocenter trial
- National/International: National

**Inclusion Criteria**

- Gender: Both, male and female
- Minimum Age: 20 Years
- Maximum Age: 40 Years

**Additional Inclusion Criteria**

- Hyperthyroidism: healthy volunteers
- Hypothyroidism: patients under thyroxine substitution

**Exclusion criteria**
any severe general disease, no cardovascular diseases

Addresses

Primary Sponsor

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Sources of Monetary or Material Support

Public funding institutions financed by tax money/Government funding body  
(German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)
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Status

- Recruitment Status: Recruiting complete, follow-up complete
- Study Closing (LPLV): 2016/06/10

Trial Publications, Results and other documents

  Brabant G, Münte TF. Partial withdrawal of levothyroxine treated disease leads to
  brain activations and effects on performance in a working memory task: A pilot

  Sartorius A, Brabant G, Münte TF. Experimentally induced subclinical
  hypothyroidism causes decreased functional connectivity of the cuneus: A
  resting state fMRI study. Psychoneuroendocrinology. 2019 Apr;102:158-163. doi:

  TF. Mild Thyrotoxicosis Leads to Brain Perfusion Changes: An Arterial Spin
  PubMed PMID: 27859916.

- Paper Göttlich M, Heldmann M, Göbel A, Dirk AL, Brabant G, Münte TF.
  Experimentally induced thyrotoxicosis leads to increased connectivity in
  PubMed PMID: 25808701.

- Paper Pietzner M, Engelmann B, Kacprowski T, Golchert J, Dirk AL, Hammer E,
  Iwen KA, Nauck M, Wallaschofski H, Führer D, Münte TF, Friedrich N, Völker U,
  Homuth G, Brabant G. Plasma proteome and metabolome characterization of an
  PMC5220622.