DFF FSS grant 2014

Project title

Towards individualized deep brain stimulation treatment of chronic neuropathic pain.

Grant holder

Professor Jens Christian H. Sørensen, Dept. of Neurosurgery, Aarhus University Hospital

Project description

The proposed project aims to provide efficient treatment for chronic pain patients beyond reach of conventional therapy. We will test the following three hypotheses:

- 1. That deep brain stimulation (DBS) treatment of the cingulate cortex effectively alleviates pain for refractory sufferers
- 2. That functional brain imaging (PET) and new non-invasive magnetic brain stimulation testing can be used to optimize patient selection for surgery and individualize DBS treatment for maximum effect and patient safety
- 3. That neuromodulation reduces blood flow and increases analgesic opioid binding in pain centres in the brain.

The collaboration unites expertise from Stanford University, California Pacific Medical Center Research Institute and several departments at Aarhus University Hospital to achieve these goals. The project facilitates exchange of professors and junior research talents between the institutions and is approved by all relevant competent authorities.

Project design

We will include 10 patients with refractory chronic pain recruited from the Pain Clinic at Aarhus University Hospital (Professors Troels Staehelin Jensen and Jens Christian H. Sørensen) and 10 control subjects. Each participant will undergo baseline clinical examination, including pain mapping, quantitative sensory testing and questionnaires at the Danish Pain Research Centre. For each participant, we will then conduct initial baseline H215O PET imaging, immediately followed by 60 minutes of focused transcranial magnetic stimulation towards the dACC region and then post stimulation repetition of the H2150 PET scan. We will conduct thermal pain stimulation to obtain a measurable pain response if necessary. Clinical pain response will be measured using the visual analogue scale. Two to seven days later, we will conduct an equivalent experiment on the same participant using 11C-Carfentanil as a PET radiotracer instead of H2150. Both experiments will be conducted at the Dept. of Nuclear Medicine and PET Centre and Danish Neuroscience Centre at Aarhus University Hospital. The experiments will provide baseline (preoperative) PET data to be used for later predictive analysis of each patient's expected outcome of deep brain stimulation. We will then measure baseline PET activity in the dACC region of interest and paired changes of this measure induced by magnetic stimulation, using the standard algorithms for PET analysis. Results will be correlated to the participant's subjective pain reporting which will also be used to classify each participant as a responder or non-responder to dACC magnetic stimulation. This information will be used for later predictive purposes related to deep brain stimulation.

The project is approved by the Danish National Committee on Health Research Ethics, the Danish Health and Medicines Authority and the Danish Data Protection Agency. The protocol complies to the guidelines for Good Clinical Practice (GCP), and the project will be monitored by the GCP unit at AU.

Project Status

Project has begun Q3 2014 with recruitment of patients and controls.

Project staff

<u>Chief investigator</u>: Professor Jens Christian H. Sørensen, Dept. of Neurosurgery, Aarhus University Hospital, jenssore@rm.dk

Co-investigators:

Professor Troels Staehelin Jensen, Dept. of Neurology, Aarhus University Hospital Associate Professor Nanna Brix Finnerup, Dept. of Neurology, Aarhus University Hospital Professor Jørgen Frøkiær, Dept. of Nuclear Medicine and PET Center, Aarhus University Hospital Assistant Professor Anne Marlene Landau, Dept. of Nuclear Medicine and PET Center, Aarhus University Head of Chemistry Dirk Bender, Department of Clinical Medicine, PET-Center, Aarhus University Hospital Chemist Anna C. Schacht, Dept. of Nuclear Medicine and PET Center.

International co-investigators:

Professor Michael C. Rowbotham, California Pacific Medical Centre Research Institute, Sutter Heath, San Francisco, CA, USA Associate Professor David C. Yeomans, Dept. of Anesthesia, Stanford University Hospital, USA.

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<u>Project nurse</u>: Anne Lene Høst Knudsen

<u>Research year students</u>: Christina E. Dahl (1/2-2014-31/1-2015) Frederik L. Hansen (1/2-2015-31/1-2016)

<u>Project administration</u>: Anja Kobberø Anne Sofie Møller Andersen

Links Links will follow.