ADEX

Preserving quality of life, physical health and functional ability in Alzheimer's disease: The effect of physical exercise

Alzheimer's Disease

Alzheimer's Disease (AD) involves cognitive and functional impairment, such as impaired learning ability, perception, memory, language and motor tasks. As AD progresses the conditions worsen, and ultimately leads to the death of the patient.

Patients with AD typically have notable mood swings, due to the cognitive implications, and they become irritable and aggressive during the later stages of disease. This imposes a lot of stress on relatives and caregivers and coupled with loss of memory, communication becomes difficult, if not impossible.

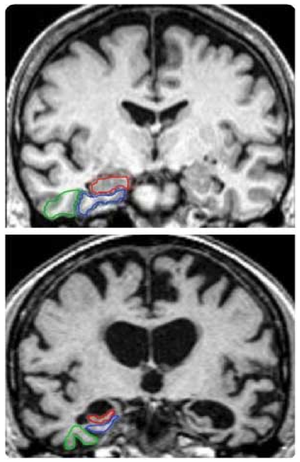
AD has no cure, and the exact cause is currently unknown. Factors, that make it highly relevant to find ways to improve the patient's quality of life, physical health and functional ability, in order to make the disease more tolerable for both patient and caregivers.

MOTIVATION

A limited set of studies have indicated that regular, physical exercise may help the patient, but all studies are inconclusive due to lack of patients or lack of control with setup parameters.

One of the primary observations in AD is an increased accumulation of amyloid-beta in the brain. The exact role of amyloid-beta wrt. the disease is still debated (cause vs. symptom), but it is suggested that reduced amyloid-beta accumulation may have positive implications. No previous studies have validated how physical exercise affects accumulation of amyloid-beta.

AD is associated with major atrophy in the brain, especially during the later stages of the disease. Several regions of the brain are affected, and the cause is loss of neurons and synapses. This emphasizes the importance of methods that can be used to accurately measure brain atrophy.



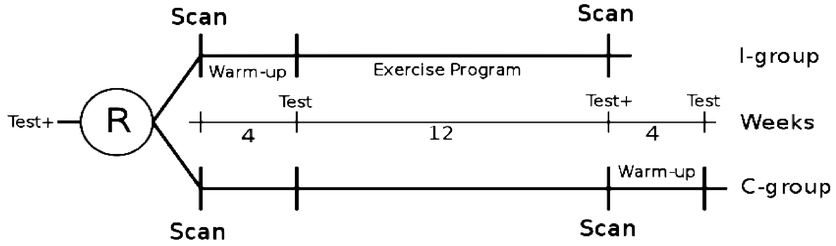
Experimental Setup

The ADEX project aims to explore how physical exercise can improve the life of patients with AD, as well as its effect on the disease itself. The project is undertaken from Rigshospitalet, but is partitioned into several sub-studies, where one is concerned with methods for Magnetic Resonance Imaging (MRI). This sub-study is a joint effort between the Technical University of Denmark (DTU) and the Danish Research Centre for Magnetic Resonance (DRCMR) located at Hvidovre Hospital.

192 patients from eight memory clinics across Denmark participate in the ADEX project, and 48 patients will be scanned before and after the exercise program at DRCMR.

Several pulse sequences are used under the MR scanning, thereby obtaining several image modalities: T1 and T2 weighted images; Fluid Attenuated Inversion Recovery (Flair) images; resting state functional MRI (fMRI); Diffuse Tensor Imaging (DTI); and Arterial Spin Labeling (ASL). The sequences run for a total of 70 minutes per scan session.

All trials in the study are randomized and blinded. The trials that are combined with MR scans are performed February 2012 – July 2013. Each round of trials runs for approximately half a year.



PHYSICAL EXERCISE SETUP

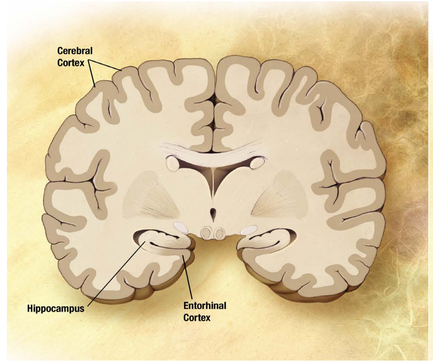
Test: Timed Up-and-Go (TUG). TUG dual tasking – count down from 50. Åstrand Rhyming test. Physical evaluation questionnaire (PASE). 400 m walk. Sit-to-Stand.

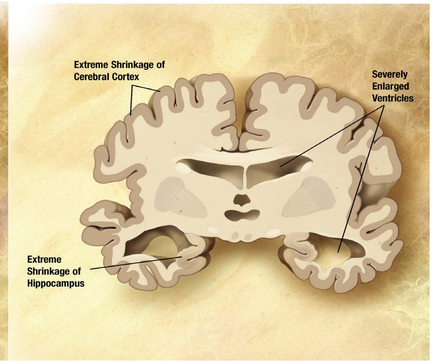
Test+: VO2max (Åstrand Rhyming). Test of muscle strength and power.

Warm-up: Introduction to exercise and individual adjustments of exercise program.

Exercise Program: Three one-hour sessions per week. 20 minutes for warming up and down, 3x10 minutes of exercise (Borg 14-16) with a 2 minute start up exercise (Borg 10-12) and a 2 minute pause between each 10 min. interval.

Study





The focus of the study will be centred on methods that utilize generative models for image segmentation, with pre-processing steps such as image registration, tissue classification and bias-field correction, in order to explore possible ways to improve data analysis in AD. In particular current methods for Voxel-Based Morphometry (VBM) will be explored.

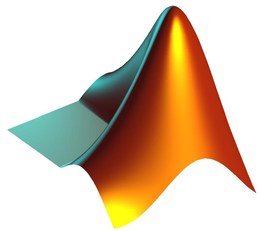
DATA AND GOALS

An attempt will be made to optimize methods for VBM analysis of AD diagnosed patient data that are currently used at DRCMR.
This requires close examination of the individual pre-processing steps, a study of current knowledge of generative models and a consequent prototype (re)-implementation of methods for VBM.

The ADEX-MR-study is longitudinal in nature with a relatively small pool of subjects (24 control, 24 intervention), as each patient is scanned twice during approximately half a year.
An attempt will be made to take advantage of this data setup, by improving the sensitivity and reliability in the generative modelling methods used for VBM by use of explicit temporal modelling.

As a final goal, image-based prediction models will be applied across image modalities in an attempt to predict the state of Alzheimer's disease in patients that exercise regularly, as well as those that do not.

The statistical significance of all results will be evaluated. This includes structural and functional effects of exercise on the brain, standard vs. optimized method performance and results obtained by use of non-temporal vs. temporal modelling as well as prediction-based modelling.



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