

Predicting prognosis in asymptomatic subjects with multiple sclerosis-like brain lesions using cognitive testing and advanced magnetic resonance techniques

The project goal

Brain magnetic resonance (MR) is a major diagnostic tool in neurological disease. Due to its high accuracy brain MR has the capacity to reveal the cause of patient's symptoms (e.g. brain tumour) but on many occasions may show findings of unclear clinical significance, so called incidental findings. MR findings typical of multiple sclerosis (MS) are particularly challenging to interpret if they occur in subjects who never had a history of neurological symptoms typical of MS, such as weakness or visual disturbances, and underwent brain MRI for other reasons, e.g. after head trauma. These subjects are currently diagnosed with radiologically isolated syndrome (RIS). Current knowledge indicates that a subset of RIS subjects have subclinical MS, others might have an alternative diagnosis or no chronic disease at all. Due to lack of biomarkers classifying an individual subject into one of these groups is currently not possible.

The aim of this project is to:

- 1) Identify RIS subjects using cognitive testing and nonconventional MR who despite being asymptomatic show the evidence of damage to the nervous system. Nonconventional MR analysis of the brain and the spinal cord will include the assessment of brain structure volumes (e.g. thalamus), integrity of neural pathways, metabolite concentration, spinal cord cross-sectional area and myelin concentration in different regions of interest.
- 2) Identify features of incidental brain lesions (e.g. location, number, size) on clinical MR which associate with hidden damage in the nervous system as revealed by cognitive testing and nonconventional MR imaging and spectroscopy
- 3) Identify hidden subgroups in the RIS cohort using unsupervised machine learning on multiple nonconventional MR features to propose classification of RIS and guide treatment decisions
- 4) Identify nonconventional MR features in the brain and the spinal cord which would predict that a RIS subject will develop MS symptoms in the next 24 months

Description of research

The study will recruit 30 RIS subjects, 25 patients with clinically definite MS and 20 healthy controls who will undergo two non-conventional MR examinations of the brain and the spinal cord at an interval of 24 months. Prior to each scan subjects will be assessed with a battery of cognitive tests. MR experiments will be carried in the Laboratory of Brain Imaging at the Nencki Institute of Experimental Biology, Polish Academy of Sciences in Warsaw, who has experience in non-conventional imaging and spectroscopy, and advanced techniques of image analysis and statistical analysis.

Reasons for attempting a particular research topic

Currently RIS subjects do not receive treatment that would slow down the disease course of MS although around half of them will ultimately develop MS symptoms in the future. There is therefore a compelling need for better characterisation of RIS group which would allow offer treatment to those with asymptomatic MS and prevent long-term disability progression.

Substantial results expected

We expect that the study will identify cognitive and nonconventional MR measures which will confirm nervous system damage in a subset of RIS subjects. We expect that some of these markers will help predict which RIS subjects develop MS symptoms in the future. We will also identify subgroups within the RIS group to propose classification guiding clinicians on how to manage RIS subjects to prevent long-term disability.