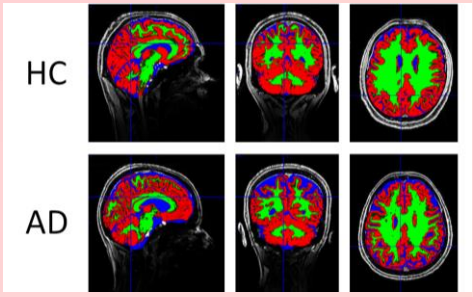
NEUROMET2 NEWSLETTER WP2 – MRS & MRI

Spring 2022

THE NEUROMET2 PROJECT

NeuroMET2 develops metrological tools to improve accuracy of diagnosis of Alzheimer's and other neurodegenerative diseases and underpin the clinical uptake of new diagnostic tests.



Segmented brain images of a healthy control (HC) and an Alzheimer's patient (AD). The increasing amounts of cerebrospinal fluid (CSF), depicted in blue, in the brain of an AD patient, and the thinning of the cortical gray matter, depicted in red, is called atrophy and a typical clinical sign in Alzheimer's Disease. White matter is depicted in green.

BACKGROUND

It is well documented that alterations of the brain occur many years before the onset of cognitive symptoms such as memory loss. Investigating the brain structure and metabolism throughout different stages of a neurodegenerative disease with quantitative, non-invasive methods, such as magnetic resonance (MR) spectroscopy and imaging, will improve the understanding of the underlying mechanisms of the disease, and may lead to new tools for early diagnosis.

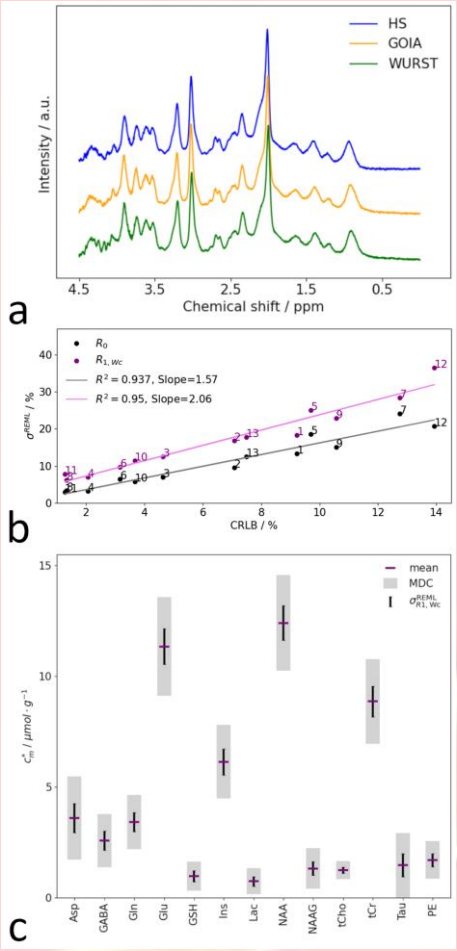
How does NeuroMET help to provide accurate diagnosis through quantitative MR spectroscopy and imaging?

Structural MR imaging has been applied in the diagnosis of Alzheimer's disease for several years as one of several diagnostic tools. The focus is often on the size of the hippocampus and atrophy in a few distinct brain regions. Furthermore, research in the past has shown that Alzheimer's disease is also accompanied by changes of metabolite concentrations in brain tissue, which can be assessed using MR spectroscopy. However, these atrophies and metabolic changes are subtle and hard to unambiguously identify in early stages of the disease, as the variances within healthy cohorts are often larger than the difference of the mean between healthy controls and patients in the early stages of the disease. For proper interpretation of the data, it is therefore important to understand which fraction of the variance within a certain patient cohort is the result of measurement uncertainties, and which fraction is resulting from actual biological variation.

While it is widely accepted that the use of ultrahigh field MR scanners, and the associated increased spectral and image resolution that can be achieved, leads to a decrease of measurement uncertainty, the actual measurement uncertainty of structural volumes and metabolite concentrations obtained from MR imaging and MR spectroscopy has so far not been determined.

To estimate the measurement uncertainty of standard laboratory measurements, usually the same measurement is repeated on the same sample several times. This is, however, not possible for in vivo MR spectroscopy or imaging within a clinical setting, as the examination is time consuming and cost intensive.

EMPIR EURAMET
The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States



a) MR spectra acquired using three different sequence variants, that were compared with regard to repeatability. b) Correlation between Cramér-Rao Lower bounds (CRLBs), and the standard deviations for repeatability (gray) and reproducibility (purple), obtained with the new REML framework for 13 metabolites. c) Mean concentrations of neurometabolites in µmol/g along with the determined respective standard deviation (black) and minimum detectable changes (gray).

Therefore, within the NeuroMET project, a study design and statistical framework was developed, that allows for the first time proper estimation of the measurement uncertainty of metabolite concentrations obtained from in vivo MR spectroscopy measurements.

Restricted Maximum Likelihood Analysis – A framework that can be transferred to other MR modalities

To investigate the measurement precision and calculate a minimally detectable change for concentrations of different brain metabolites measured in vivo, healthy volunteers were examined four times: twice on day one, with a break between examinations, and twice a week later without a break between examinations. Using a restricted maximum likelihood (REML) model it was possible to extract the measurement uncertainty of the metabolite concentrations measured in vivo. While the obtained results are so far only applicable to the setup used within the NeuroMET project, the framework is easily transferrable to investigate the measurement uncertainty of other setups – i.e. different MR scanners, sequences, and processing workflows – as well as other modalities – i.e. different examination techniques. Hence, this framework is a crucial step toward systematically reducing measurement uncertainty and increasing reliability and diagnostic value of quantitative MR spectroscopy and imaging examinations.

The full paper can be found here: https://doi.org/10.1002/mrm.29034

For further information about the NeuroMET2 project, please visit https://www.lgcgroup.com/our-programmes/empir-neuromet/

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