A Clinical Decision Support system based on Quantitative multimodal brain MRI for personalized treatment in neurological and psychiatric disorders

Reporting

Project Information

CDS-QUAMRI
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Project website

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Periodic Reporting for period 1 - CDS-QUAMRI (A Clinical Decision Support system based on Quantitative multimodal brain MRI for personalized treatment in neurological and psychiatric disorders)

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Summary of the context and overall objectives of the project
A large number of neurological disorders (multiple sclerosis (MS), early dementia / mild cognitive impairment (MCI) vs. early Alzheimer’s disease, migraine, chronic pain, mild traumatic brain injury) and psychiatric disorders (major and bipolar depression (MDD / BD), schizophrenia, obsessive-compulsive disorder (OCD), addiction, anxiety, attention deficit hyperactivity syndrome (ADHS), posttraumatic stress disorder (PTSD)) lack objective criteria for primary diagnosis, early differential diagnosis with regard to subtypes in treatment response and disease progression or effective therapy monitoring. Correct diagnoses at early stages and correct patient stratification are hence often severely delayed and patients are left without any appropriate treatment for years resulting in a tremendous negative socio-economic impact. In contrast to many clinical disciplines, neither predictive physiological biomarkers nor imaging-based surrogate markers have been established yet. However, scientific studies based on advanced MRI methods indicate that patients with the above mentioned neurological and psychiatric disorders show specific subtle changes in multiple MRI readouts that are only detectable by quantitative approaches. So far little effort has been put to overcome known methodological limitations especially in analysis and quantification of multi-modal MRI data to exploit this knowledge for clinical decision-making.

Hence a clinical decision support system (CDS) enabling personalized diagnostics and treatment for neurological and psychiatric disorders is envisioned that is based on multimodal quantitative (QUA) magnetic resonance imaging (MRI) and multi-parametric classification and shall be demonstrated for major depressive disorder (treatment response prediction) and multiple sclerosis (disease progression type prediction).

**Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far**

One objective of the CDS QUAMRI project is to fully integrate advanced analysis algorithms of multi-modal structural, functional and metabolic MRI data into a single software framework to make them accessible for non-expert clinical users in order to allow for large scale clinical trials and more widespread use in neuroscience as a basis for the future use in clinical decision making. The quantification and feature extraction algorithms for magnetic resonance spectroscopic imaging (MRSI), diffusion weighted imaging (DWI), resting-state functional MRI (rs-fMRI) and perfusion imaging (arterial spin labelling (ASL)) shall be enhanced to access the full information content of the data at high reliability as required for future use in diagnostics, stratification and monitoring of patients.

During the first funding period the consortium made progress towards this objective by jointly establishing a comprehensive software development plan, by defining the core structure and internal data format of data analysis modules and by implementing a data base that serves as software framework for data and analysis workflow management and visualization. In parallel and as preparatory step towards integration of all MRI data analysis modules into the data management software framework the adoption of existing MRI analysis modules (fMRI / ASL, DWI) to suit the interface of the data management frame and the implementation of new MRI analysis modules (MRS, Relaxometry) by integration of existing tools and algorithmic implementations in line with the core
structure and internal data format as mentioned above have been started.

The second objective of the CDS QUAMRI project is to develop a prototype Clinical Decision support system using classifiers that discriminate different patient subgroups (treatment response, disease progression) using machine-learning based classification methods and pre-existing multi-modal MRI data from patients with major depressive disorder as well as multiple sclerosis.

During the first funding period pre-existing multi-modal MRI data from patients with major depressive disorder, multiple sclerosis and healthy volunteers were pooled, re-analyzed and respective features were extracted as input into the classifier development. First successful classifiers have been developed that allow for retrospective classification of patient sub-groups. These classifiers shall be refined to further enhance specificity and sensitivity in order to allow for prospective classification of single patient data sets in future. In addition, the MRI scan protocol for a prospective multi-modal MRI study in depressive subjects has been developed, institutional review board (IRB) approval has been obtained and the study has been started.

Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the project so far)

We aim at the first software solution that offers full integration of a reconstruction, processing and quantification pipeline for 11 MRI modalities into a common data handling, visualization, feature extraction and classification framework. The 11 MRI modalities include: anatomical MRI (aMRI), quantitative T1 (qT1) and T2 (qT2) relaxation rate measurements myeline water imaging (MI), task-based functional MRI (task-fMRI), resting-state functional MRI (rs-fMRI), diffusion weighted MRI (DWI), perfusion imaging by arterial spin labelling (ASL), magnetic resonance spectroscopic imaging (MRSI), chemical exchange saturation transfer imaging (CEST) and non-proton imaging (xMRI). In addition, further development of the quantification and feature extraction algorithms for different advanced MRI modalities (MRSI, rs-fMRI, DWI, MI, ASL) as well as the development of a machine learning based classification approach is envisioned to maximize the amount of information that can be extracted. This effort will all but enable the more widespread use of multimodal quantitative MRI in neuroscience and large clinical trials, which in turn are the basis for future application of advanced MRI in clinical decision making with regard to a large number of neurological and psychiatric disorders.

The envisioned classification based Clinical Decision Support System will be a step changer in diagnostic MRI. It shall make use of yet to determine disease specific MRI based surrogate markers to enable (1) unambiguous early diagnostics of a significant number of neurologic and psychiatric disorders that so far lack objective diagnostics criteria, (2) the distinction of different patient subgroups responding in a different manner to a specific treatment (for instance major depression or chronic pain) or having different disease progression perspectives (for instance early schizophrenia or multiple sclerosis) and related monitoring and (3) to use this information on a case by case basis in clinical decision making in order to facilitate personalized treatment without the need for repeated unnecessary trials with inefficient treatment forms for the first time.
So far the concept of using machine learning on MRI data for distinguishing patient subgroups in major depressive disorder and multiple sclerosis has been successfully tested, but needs further work to enable true Clinical Decision Support in the single patient case. Good progress on the software implementation and integration side has been achieved with partly novel and quantitative analysis algorithms that have been developed and a data and work flow management software framework that has been almost completed. However the fully integrated software solution will be available only at a later stage of the project.