Dementia modelling

Rendicontazione

Informazioni relative al progetto

DEMO

ID dell'accordo di sovvenzione: 721820

Sito web del progetto

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10.3030/721820

Progetto chiuso

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Sintesi del contesto e degli obiettivi generali del progetto

Dementia constitutes a major burden on society, both in monetary costs and the suffering of patients and relatives. Alzheimer's disease (AD), the most common form of dementia, is one of the most devastating healthcare problems faced by western society. The prevalence increases with the

average lifetime year by year, and in most countries the population is aging.

Different types of dementia require different treatments. Cardiovascular treatments may, e.g. prevent or slow vascular dementia (VaD), which is the second most common type of dementia. There are currently no disease-modifying treatments for AD, despite numerous promising drugs in development. Another challenge is that many of the dementias have clinically similar presentations and may co-exist (as many as 50% of AD patients may have VaD as well), making clinical diagnosis challenging. However, signs of dementia-related pathology are measurable using biomarkers far before clinical presentation, and the various types of dementia have quite different pathological bases.

The overall objective of the Dementia Modeling (DeMo) project is to develop new models for AD, VaD and mixed AD and VaD progression using, among others, novel imaging biomarkers of vascular pathology alongside already established AD imaging biomarkers. Such models enable identification and differentiation of at-risk subjects for effective treatment, and they can be used to assess disease progression for among others treatment monitorization.

The project emphasizes the use of historically widely used MRI scan types to enable use of historical imaging data in modeling. Algorithms are simultaneously developed for (1) robust disease progression modeling, and for the underlying necessary brain imaging biomarkers of VaD to be measured at each time point and entered to the disease progression model; i.e. (2) white matter lesion imaging biomarkers and (3) vascular pathology imaging biomarkers.

Three early stage researchers (ESRs) are trained while performing these three objectives (1-3) of the project.

Lavoro eseguito dall'inizio del progetto fino alla fine del periodo coperto dalla relazione e principali risultati finora ottenuti

The individual ESRs drive the progress of each of the respective objectives of the project, (1) robust disease progression modeling, (2) imaging biomarkers of white matter pathology, and (3) imaging biomarkers of vascular pathology. The ESRs each produced from project start to end of the current reporting period results that were disseminated by different means. Scientific posters and/or oral presentations were presented at summer schools, workshops, and international conferences. Clinical abstracts were published at clinical conferences. Conference or workshop papers were published at international workshops and conferences. Journal papers were published top medical and neuroimaging journals.

The main results within each of the 3 objectives are:

Objective 1

1a) A new method for training recurrent deep neural networks while gracefully handling missing data which is an often-occurring problem. For details, see this paper https://arxiv.org/pdf/1903.07173

and video https://youtu.be/k1xKKlvY14k.
1b) A new method for parametric modeling of disease progression robust to outliers which are often occurring in real-world longitudinal data. For details, see this paper https://doi.org/10.1016/j.neuroimage.2020.117460.
1c) A new initialization method that addresses the training instability of long short-term memory (LSTM) networks. This results in better trained networks. For details, see this paper https://arxiv.org/pdf/1912.10454 and video https://dementia-modelling.eu/wp-content/uploads/2020/01/ICONIP2019-Mostafa.mp4.

Objective 2

2a) A new method for using specialized MRI sequences to steer the training of deep neural networks for white matter lesion segmentation in standard MRI sequence types. This results in better trained networks. For details, see this paper https://arxiv.org/pdf/1808.05500.
2b) A new method for artificially extending the training data for deep neural networks by deformations to address that suitable training data is often scarce in real-world scenarios. For details, see this paper https://arxiv.org/pdf/1810.01928.
2c) Two new methods for training deep neural networks to better generalize to MRI data from new data sources with different characteristics (e.g. different scanners) without need for labeled data examples from the new data source – something that is often costly, or even impossible, to get in many real-world situations. For details, see these papers https://arxiv.org/pdf/1908.07355 and https://arxiv.org/pdf/1908.05959.

Objective 3

3a) A new method for handling extreme data imbalance when training a deep neural network for segmentation of microbleeds in standard MRI sequence types. Classical approaches fails to detect small and rare structures such as microbleeds, as it is more cost-effective for an algorithm to miss such structures all the time rather than over-segment them. The proposed approach that relies on the key machine learning concept curriculum learning will be presented at a medical imaging conference in 2021 (https://spie.org/MI/conferencedetails/medical-image-processing Paper 11596-4).

Progressi oltre lo stato dell'arte e potenziale impatto previsto (incluso l'impatto socioeconomico e le implicazioni sociali più ampie del progetto fino ad ora)

Progress beyond state-of-the-art for the three project objectives is

Objective 1

The new method 1a) makes training less influenced by missing data, and it can be applied to different types of recurrent neural networks without any need for changing these which makes it widely applicable. Moreover, contrary to the state-of-the-art, this method does not try to learn and utilize re-

occurring missing value patterns, but instead tries to learn the true disease progression signal in the data. 1b) Advances state-of-the-art parametric disease progression modelling by allowing better training in situations with outliers in the data and/or asymmetric monotonic biomarker progression. 1c) is expected to have substantial influence on the training of the most widely used recurrent neural networks, LSTM networks, since initialization rules not designed and inappropriate for these are often used.

Objective 2

The new method 2a) allows incorporating more advanced MRI sequence types during training to arrive at a better trained model, but without the need for these MRI sequences when the trained model is applied. State-of-the-art does not rely on the simple MRI sequences, but instead require the advanced as input when the model is applied, limiting the applicability in cohorts that does not have these. 2b) and 2c) will generally, by better training, improve performance of deep learning methods for application in both known and so far unseen cohorts. The latter is expected to significantly advance the clinical applicability of these methods.

Objective 3

The new method 3a) will improve the training of deep neural networks for micro-bleed segmentation – a notoriously hard problem to optimize for due to the imbalance in the presence of positive cases (micro-bleeds) vs. negative cases (normal appearing brain tissue) caused by both few micro-bleeds in general and their small size. Moreover, the methods showcase that micro-bleed segmentation can be realized in an MRI sequence (T2*) that has traditionally been used in neurology.

The goal of the Dementia Modelling (DEMO) project

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