MRI Segmentation of brainstem structures using Deep Learning techniques: Application to Amyotrophic Lateral Sclerosis

Context

Required profile: Master or Engineering degree in Machine Learning, Data Science, or Medical Imaging.
Required skills: Knowledge of Deep Learning for imaging in Python, image processing, and a strong statistical background
Thesis Directors: Pr. Jérémie Sublime (ISEP) & Dr. (Pr.) Véronique Marchand-Pauvert (LIB, INSERM U1146)
Workplaces: ISEP campus (Issy-Les-Moulineaux, 92), La Pitié-Salpêtrière Hospital (Paris, 13arr)

Project

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease affecting motor neurons in the central nervous system, leading to progressive paralysis and death within 2-5 years after the first symptoms, most often due to respiratory failure. There is no therapy with a satisfactory effect on survival and quality of life. The diagnosis is usually long (12-18 months), thus delaying a proper follow-up and possible inclusion in clinical trials. Furthermore, assessing the prognosis of patients (rapid or slow progression, response to innovative therapies) is currently difficult with clinical routine. However, several studies have shown that multimodal magnetic resonance imaging (MRI) gives rise to valuable biomarkers and metrics for patient evaluation and prognosis [1][2].
Among the structures of the central nervous system, and more especially the brainstem is of particular interest in ALS. It is located between the brain and the spinal cord, and englobes motor neurons that are crucial for patient survival (respiratory control). Accordingly, it has been shown that atrophy of the brainstem lower part, quantified using anatomical MRI, helps to predict respiratory failure (before the first symptoms) and anticipate its clinical management [3]. However, to date, no methodology exists for a fine segmentation of brainstem structures, especially to distinguish between white (myelinated axons –emerging from neurons– supporting structural connectivity between populations of neurons) and grey matter (structures grouping neuron cell bodies, called nuclei). The thesis project is therefore to investigate the potential of Deep Learning methods on multimodal MRI data of ALS patients in order to: a) achieve a precise segmentation of the brainstem and the delineation of brainstem nuclei and white matter, b) assess the effect of the disease and studying the underlying mechanisms on the discovered structures by comparing MRI data of control subjects and patients at more or less advanced stages, c) proposing a method to classify healthy and sick subjects and to predict the stage of the disease, and hopefully d) predict the evolution of ALS from early exams.

Objective a) will be key to segment and extract key features of different areas of the brainstem affected by the disease. In turn, this could be used to understand the underlying mechanisms and achieve step b) and c) with a method able to distinguish between healthy subjects and patients but which could also help determining the stage of the disease. Finally, the last objective is to predict how the disease may evolve -if successful- may lead to important breakthroughs in assessing the effectiveness of trial drugs for ALS.

Challenges

Challenges for this project are numerous:

a) While the brainstem has been identified as one of the areas primarily affected by ALS, it remains difficult to segment using multimodal MRI data due to the poor spatial resolution and the low contrast of the images. For these reasons, in this PhD thesis, we propose to train deep neural networks on subcortical brain areas such as thalamus and basal ganglia, for which annotations (in terms of distinction between grey and white matter) are more easily available.

b) Deep Learning method tend to require very large amounts of reliably annotated data. The datasets proposed by the INSERM partner and La Pitié-Salpêtrière are SOMALS and PULSE, which contain around 53 and 500 patients respectively, under various modalities MRI (T1 and diffusion). These numbers are somewhat low for fully supervised methods. Furthermore, annotations are also scarce and rely mostly on atlases. This will a major challenge for the segmentation step and predicting the evolution of the disease. Solving this problem could require a mix of unsupervised deep learning [4], and the development of new algorithms that can be trained from unlabeled data while integrating a few reliably labelled examples for guidance. Recent progresses in self-supervised learning methods in both remote sensing [5] and medical images [6] for segmentation and classification purposes makes us optimistic that it can be done.

c) The last challenge will be concerned with the predictive aspect using very short time series, as time series related with ALS patient tend to be short due to the somewhat fast nature of the disease and relative cost of MRI exams.

It is worth mentioning, that while the PhD candidate will be a computer scientist working on a Machine Learning problem, finding reliable and interpretable models for the evolutions of ALS may lead to breakthroughs in finding more effective medical treatments for ALS as a successful model may help to determine whether or not a treatment changes the course of the lesion evolution.

References:

[1] Querin G. et al.: Multimodal spinal cord MRI offers accurate diagnostic classification in ALS. J Neurol Neurosurg Psychiatry. 2018;89(11):1220-1221.

[2] Grolez G. et al.: The value of magnetic resonance imaging as a biomarker for amyotrophic lateral sclerosis: a systematic review. BMC Neurol. 2016;16(1):155.

[3] Grolez G. et al.: MRI of the cervical spinal cord predicts respiratory dysfunction in ALS. Sci Rep. 2018;8(1):1828.

[4] Royer C. et al.: Unsupervised Approaches for the Segmentation of Dry ARMD Lesions in Eye Fundus cSLO Images. J. Imaging 7(8): 143 (2021)

[5] Li Yu et al.: Deep Self-Supervised Learning for Few-Shot Hyperspectral Image Classification. IGARSS 2020 - 2020 IEEE International Geoscience and Remote Sensing Symposium, 26/09-02/10/2020, Waikoloa, HI, USA.

[6] Ouyang C. et al: Self-Supervised Learning for Few-Shot Medical Image Segmentation. IEEE Trans Med Imaging. 2022 Jul;41(7):1837-1848. doi: 10.1109/TMI.2022.3150682.

Collaborations

This thesis project will be done within the context of a collaboration between ISEP and the Neuroscience team of the LIB, INSERM U1146, working at Paris La Salpêtrière Hospital. Dr. Véronique Marchand-Pauvert will be the co-director of this PhD thesis and the main contact with medical teams.