PROJECT 1

DoS: Elisa Canu

Title: Individual phenotipic characterization of patients within the frontotemporal lobar degeneration/motor neuron disease spectrum using multimodal MRI

Curriculum: Neuroscience and Experimental Neurology

Link to OSR/UniSR personal page: http://research.hsr.it/en/institutes/institute-of-experimental-neurology/neuroimaging-research/elisa-canu.html

Project description (*Number of characters*, *including spaces*: 2.000 - 3.000):
Neuroimaging studies are emphasizing the idea that the Frontotemporal lobar degeneration (FTLD)/Motor Neuron Disease (MND) represents a specific neural system disease. FTLD encompasses a wide spectrum of clinical syndromes ranging from the behavioral variant of frontotemporal dementia (bvFTD) to primary progressive aphasia (PPA) and progressive supranuclear palsy syndrome (PSPs). MND share clinical and neuropathological features with FTLD-related syndromes. Distinguishing between FTLD/MND phenotypes is important with the emergence of therapies targeted to specific disease mechanisms. For MRI to be useful in the clinical setting, studies on large, independent, clinically and biologically well-characterized FTLD/MND populations are needed in order to improve our understanding of the clinical heterogeneity of the disease and define multimodal MRI markers to be applied for individual patient classification. The integration of different MRI modalities (i.e., structural, diffusion tensor [DT], and resting state [RS] functional MRI) identified commonalities and differences of these syndromes. However, the results of previous studies have had a minimal clinical impact since they reported results at group rather than at individual subject level. In order to translate research findings to clinical practice, an individual patient classification is needed. In this study we will investigate common and specific structural and functional brain MRI features of independent samples of patients within the FTLD/MND spectrum. Both sporadic and genetic cases will be involved. Defined brain MRI features will be useful for classifying new recruited FTLD/MND cases and for characterizing their disease progression over 3 years. The results of this study will also lead to define a standardized MRI protocol with immediate translation to the clinical practice.
In two independent, previously recruited cohorts of FTLD/MND patients, this study aims 1) to identify the patterns of GM atrophy, WM tract damage and functional connectivity alterations reflecting the FTLD/MND continuum, as well as the phenotype specific brain signatures using the complementary information derived from 3D T1 images, DT MRI and RS fMRI; 2) to define common and distinct structural and functional MRI features in FTLD familial compared to sporadic cases to provide the in vivo patterns of damage occurring with different genetic backgrounds; 3) to define a common MRI protocol to be applied in a multicenter, longitudinal setting in a large sample of new FTLD/MND cases in order to validate the MRI markers obtained at aims 1 and 2 and to determine their accuracy in classifying different clinical syndromes and predict disease progression.

Skills to be acquired by the student:

During the project the student will acquire the following skills:

1) Pre-processing of MRI data (structural, DTI, resting state functional MRI).
2) MRI analysis to assess brain atrophy, white matter alterations and resting state functional changes.

3) Deep learning and Supervised pattern recognition algorithms for the classification of healthy subjects and patients with frontotemporal dementia.
4) Definition of FTLD clinical and cognitive profiles associated with specific patterns of brain damage in sporadic and genetic cases.
5) Interpretation of data in patients with frontotemporal dementia.
6) Drafting of research reports and articles.

References (max. 3)

1. **Canu E**, Agosta F, Mandic-Stojmenovic G, Stojković T, Stefanova E, Inuggi A, Imperiale F, Copetti M, Kostic VS, Filippi M. Multiparametric MRI to distinguish early onset Alzheimer's disease and behavioural variant of frontotemporal dementia.
2. Agosta F, Scola E, **Canu E**, Marcone A, Magnani G, Sarro L, Copetti M, Caso F, Cerami C, Comi G, Cappa SF, Falini A, Filippi M. White matter damage in frontotemporal lobar degeneration spectrum. Cereb Cortex. 2012 Dec;22(12):2705-14.
3. **Canu E**, Agosta F, Baglio F, Galantucci S, Nemni R, Filippi M. Diffusion tensor magnetic resonance imaging tractography in progressive supranuclear palsy. Mov Disord. 2011 Aug 1;26(9):1752-5.