PROJECT 1

DoS: Federica Agosta
Title: Tracking and predicting neurodegeneration spreading across the brain connectome: understanding clinical (and presymptomatic) evolution of sporadic and genetic FTLD syndromes

Curriculum: Neuroscience and Experimental Neurology

Link to OSR/UniSR personal page: http://www.unisr.it/dottorati-2/15134-2/

Project description (*Number of characters*, *including spaces*: 2.000 - 3.000):
One of the central questions in neurodegenerative diseases is how network degeneration gives rise to the observed wide, heterogeneous spectrum of disease phenotypes. This project seeks to decipher the mechanisms of network-based neurodegeneration by understanding how the complex architecture of brain networks (the connectome) shapes the evolving pathology of neurodegenerative diseases, and to develop tools for monitoring disease progression from presymptomatic to later stages of the disease. The project will apply emerging network science tools to longitudinal, structural and functional brain connectivity 3T magnetic resonance imaging data from patients with frontotemporal lobar degeneration (FTLD) – a devastating, relentlessly progressive, young onset, neurodegenerative disorder. We will define the spatial and temporal evolution of structural and functional connectome abnormalities in different FTLD syndromes. We will characterize the progression of network changes in terms of both connection properties and node features. These experiments will allow us to answer the following crucial research questions: What are the patterns of the propagation and lateralization of network damage in diverse FTLD phenotypes? What are the rates of progression within different brain regions? What are the relative contributions of structural and functional connectivity changes to the progression of the disease? How do network changes relate to blood and cerebrospinal fluid biomarkers of neurodegeneration? We will also move beyond syndromic disease maps to *in vivo* patterns of spatial and temporal network degeneration associated with specific proteinopathies. To achieve this goal, we will apply the tools mentioned above in patients carrying FTLD-related mutations as well as in presymptomatic members of families with known pathogenic FTLD mutations to explore specifically the earliest, even presymptomatic, stages of the disease.

Skills to be acquired by the student:

The student should be a neurologist. During the project the student will acquire the following skills:

1) Pre-processing of MRI data (structural, HARDI, resting state functional MRI)
2) Interpretation of network analysis data in patients with frontotemporal dementia
3) Definition of clinico-imaging correlations in patients with frontotemporal dementia
4) Understanding the structural and functional brain correlates of clinical evolution in familial forms of frontotemporal dementia
5) Drafting of research reports and articles

References (max. 3)

Agosta F, Weiler M, Filippi M. Propagation of Pathology through Brain Networks in Neurodegenerative Diseases: From Molecules to Clinical Phenotypes. CNS Neurosci Ther 2015;21:754-767

Filippi M, Basaia S, Canu E, Imperiale F, Meani A, Caso F, Magnani G, Falautano M, Comi G, Falini A, Agosta F. Brain network connectivity differs in early-onset neurodegenerative dementia. Neurology 2017;89:1764-1772

Agosta F, Sala S, Valsasina P, Meani A, Canu E, Magnani G, Cappa SF, Scola E, Quatto P, Horsfield MA, Falini A, Comi G, Filippi M. Brain network connectivity assessed using graph theory in frontotemporal dementia. Neurology 2013;81:134-143