Divergent and convergent pathways in neurodegenerative dementias: multiparametric in vivo PET assessment of cerebral metabolism, tau and amyloid-burdens

Alzheimer’s disease (AD), Lewy Body Disease (DLB) and Frontotemporal lobar degeneration spectrum (FTLD) are brain system diseases associated to specific underlying neuropathology. The alteration of selective neural systems and connectivity can be at the basis of clinical presentations. Aβ and tau pathologies have been found in both AD and in several sub-types of FTLD. Aβ is also present in DLB, classified as synucleinopathy. PET is the only one technique for the in-vivo measurements of molecular pathophysiology (Aβ and tau burden) and synaptic dysfunction in dementia, using adequate radiotracers. Very little is known on the mechanisms underlying the regional system vulnerability to Aβ and tau aggregations and accumulation in the brain of different dementia conditions.

The main objective of this research is to explore with a PET multiparametric approach divergent and convergent pathways of brain vulnerability in different neurodegenerative dementias and correlate them with clinical aspects. This might provide new molecular knowledge and insights on causal mechanisms in dementia, and, possibly, forms an evidence base for future clinical trials.

Research activities:

i) To evaluated the altered whole-brain functional networks (i.e. brain connectome) in specific clinical subtypes (early AD, DLB, FTLD spectrum) by applying graph theoretical analyses to FDG-PET data;

ii) To investigate the in-vivo Aβ and tau spatial distributions and the changes in FDG-PET connectome in different stages of diseases (i.e. in few selected prodromal and probable cases);

iii) To test the hypothesis of the possible relationship between the network nature of Aβ distribution and the altered functional connectome in AD (amyloidopathy) and in DLB (alpha-synucleinopathy);

iv) To focus on few familial and genetic cases in the comparison between network nature of tau burden and FDG-PET neural energy dysfunction in familial AD (presenilin 1-2) and FTLD-tauopathies.
References

- Perani, D. "CURRENT OPINION FDG-PET and amyloid-PET imaging: the diverging paths." *Curr Opin Neurol* 27 (2014): 000-000