Multiparametric *in-vivo* PET measures in neurodegenerative proteinopathies

Several neurodegenerative diseases leading to dementia are associated with deposition of misfolded and aggregated proteins in the brain [1,2]. The same proteinopathy can manifest as different and distinct clinical phenotypes, and in the same way, different proteinopathies (e.g., β-amyloid, tau and α-synuclein) can cause overlapping clinical phenotypes [1,2]. Still we do not know the pathological events triggering neurodegeneration in presence of a proteinopathy. Several hypotheses focused on the interplay of numerous pathogenic mechanisms (e.g. interaction between misfolding and aggregation of amyloid and tau proteins, intracellular mitochondrial dysfunction, neuroinflammation) [1,3,4].

PET, with adequate radiotracers, is a unique tool for the *in vivo* measurements of molecular pathophysiology (Aβ and tau burdens), and synaptic dysfunction (regional cerebral hypometabolism) in neurodegenerative diseases [4].

The main objective of this research is to *in vivo* explore with a PET multiparametric approach the pathological substrates (i.e., amyloid and tau burden and neuronal dysfunction) leading to divergent and convergent pathways in neurodegeneration that might explain specific brain vulnerability. This might provide new molecular knowledge and insights on causal mechanisms of neurodegeneration, and possibly provide evidence for future clinical trials.

**Research activities:**

**Prospective and retrospective studies (local database and ADNI repository).**

**Aims:**

i) To *in vivo* investigate the relationships between cerebral Aβ amyloid and tau burdens and glucose brain metabolism, as assessed by PET in case series of Alzheimer Disease and frontotemporal spectrum

ii) To *in vivo* investigate the relationships between cerebral tau burdens and FDG brain metabolism, in the preclinical disease phase as assessed by PET in carriers of known genetic diseases (i.e. presenilin 1 and MAPT)

iii) To evaluate in small series of dementia cases with known proteinopathy (AD-tau and amyloidosis, FTD-tau) the alteration of FDG-PET metabolic functional connectivity (i.e. brain connectome) in relationship to known models of pathological protein propagation

**References**


