BRAIN IMAGING WITH MULTIMODAL PET MOLECULAR APPROACHES

Daniela Perani, MD
Vita-Salute San Raffaele University,
Nuclear Medicine Department and Division of Neuroscience San Raffaele Scientific Institute, Milan, Italy

Positron emission tomography (PET) allows *in vivo* measurements of multiple parameters of regional cerebral physiology, such as blood flow, oxidative and glucose metabolism. In addition, moving to the molecular levels of investigation, PET with adequate radiotracers is unique in the evaluation of the multiple neurotransmitter/neuroreceptor systems of the human brain. These applied studies have increased our understanding of biological and clinical aspects of neurological and psychiatric diseases and have provided information for early diagnosis of dementia conditions

These potentialities are becoming more and more important as the field of research moves to clinical applications. PET techniques have been extensively applied to the study of neurodegenerative diseases, by measuring glucose metabolism and specific targets such as dopaminergic, cholinergic, serotoninergic neurons, reactive glial cells and tau and amyloid deposits.

Main application fields:

a. The study of single cases or comparable group of patients with cognitive deficits, using the tools of cognitive neuropsychology, combined with metabolic imaging methods, such as 18F-FDG PET provided consistent patterns of hypometabolism correlated with the behavioural and cognitive modifications. Due to the very high sensitivity and specificity, PET can be used to predict the cognitive decline and progression to dementia in subjects without a clear-cut clinical diagnosis such as in Mild Cognitive Impairment (MCI). Neuroimaging and genetic testing have aided in the identification of individuals at increased risk for dementia.

   In addition, although [18F]FDG plays a major role, other tracers are becoming available, that could detect the AD pathology in subjects at risk (i.e. tracers for amyloid and tau deposits). PET imaging represents a major tool in the guidelines for the *in vivo* measurements of biomarkers of pathology (amyloid-PET) and neurodegeneration (FDG-PET). The use of PET in dementia is increasing and this is due to various factors, such as the higher accuracy of PET reading through automatic analysis (i.e. SPM) and availability of large data-bases of normal subjects.

b. PET molecular studies of brain functional reserve in groups of probable AD patients and in prodromal AD phase (MCI subjects) have shown that the level of education and occupational activity have a clear-cut neurobiological correlate, namely a functional and molecular reserve capacity probably contrasting the clinical onset and progression of dementia.

c. Neurotransmission studies by PET imaging techniques to measure the distribution of various molecular components that are at the basis of the neuronal communication, like receptors, membrane carriers, neurotransmitters and enzymes. The central nervous system controls behavioural and cognitive processes by modulating the transfer of information through complex neurochemical interaction. These interactions occur through different neurotransmitter systems to maintain homeostasis and to control each different

cognitive or behavioural process in physiological condition or their alteration during pathologies. Molecular PET imaging can be used to *in vivo* measure changes of neurotransmitters interaction in neurological and psychiatric diseases.

Here, I will provide examples from the current literature and personal data on the role of functional and molecular PET neuroimaging.