FDG and Amyloid imaging in Alzheimer's disease

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The pathophysiological hallmark of Alzheimer's disease (AD) is the accumulation of amyloid plaques in the brain with a fairly constant distribution pattern involving the basal portions of the frontal, temporal and occipital lobe with a partial saving of the hippocampal formation and primary sensory areas[1]. In vivo 2-deoxy-2-(^{18}F) fluoro-D-glucose (^{18}F-FDG) PET is a minimally invasive diagnostic imaging procedure used that evaluate cerebral glucose metabolism[2] while SPECT with 99mTc-exametazime (HMPAO) and 99mTc-bicisate (ethyl cystine dimer [ECD]) reflects regional cerebral perfusion[3]. ^{18}F-FDG PET is superior to perfusional SPECT in its ability to separate healthy controls from patients with true dementing illnesses[2] detecting functional changes that results in a reduced brain glucose metabolism due to amyloid deposition as neuronal injury and disfunction and cell death[4] .

In Mild Cognitive Impairment (MCI), different brain glucose metabolism patterns have been found between converters and non converters patients[5]. MCI converters usually show a greater brain glucose metabolism involvement in parietal, cingulated hippocampus and parahippocampus cortex as compared to MCI non converters which brain metabolic pattern is characterized by a selected involvement of dorsolateral frontal cortex[5]. It has been suggested that ^{18}F-FDG PET findings may be useful in predicting short term conversion to AD[5, 6]. Part of the previously mentioned results are obtained by means of computer-assisted quantitative interpretation of images[7], being the visual rating of functional brain ^{18}F-FDG PET images heavily dependent to the lack of clearly defined cutoffs to distinguish between normal and pathologic findings especially at the early stage of the disease [2]. Several semi-automated tools initially developed for research applications[7] have been developed (i.e. statistical parametric mapping, SPM, Wellcome Department of Cognitive Neurology, London, UK) for clinical interpretations of a large number of neurologic disorders[8]. In our experience, the application of these tools leads to a greater diagnostic accuracy, but the process is a little time consuming and images derived from different scanners and with different acquisition parameters cannot always be compared.

^{11}C labelled PET tracer (Pittsburg Compound B) PiB is the most widely used radiotracer for amyloid imaging in human beings[9]. Due to short ^{11}C half-life, three ^{18}F labelled tracers are being investigated in clinical trials for amyloid imaging. Flutemetamol (GE-067) is the 3´-fluoro-derivative of PiB , whereas florbetaben (BAY-94-9172, AV-1) and florbetapir (AV-45) are stilbene and styrylpyridine derivatives, which exhibit high affinity binding for fibrillary amyloid similar to PiB[9]. The regional retention of ^{11}C-PiB appears to be reliable to the regional density of Amiloid

plaques in AD[10]. In MCI patients, follow-up studies have shown that 70% of ^{11}C-PiB positive MCI subjects will progress to dementia due to AD over 3 years[11]. Less than 10% of ^{11}C-PiB negative MCI patients progress to a clinical diagnosis of AD, whereas about 20% of ^{11}C-PiB negative MCI subjects progress to another type of dementia such as dementia with Lewy bodies or frontotemporal dementia[11]. As a result, tracers for amyloid imaging could be helpful in early identification of MCI patients that will convert in AD[11].

In conclusion the high sensitivity and specificity of ^{18}F-FDG PET in the diagnosis of AD is implemented by software programs for the quantitative interpretation of scans especially in the early stage of the disease and when considering MCI patients. Several early reports suggest a strong predictive value of amyloid tracers for progression from MCI to AD, and this tracer could represent a useful tool in the diagnosis of AD and its differential diagnosis from FTD[2].

It is our opinion that current advances in functional imaging awaits the development of an effective therapy to slow, halt or possibly reverse the amyloid-based disease process.

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