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The use of Positron Emission Tomography (PET) in the diagnosis of neurodegenerative diseases of the elderly

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The growth expectation of dementia in the elderly leads to the search of prevention and early detection of symptoms and signs. Early diagnosis of dementia is quite relevant since the pharmacological treatments can be more effective. Patients with mild cognitive impairment (MCI) require particular attention because they can be considered at a stage that often precedes dementia. MCI patients have stronger cognitive decline than expected for the age but not severe enough to meet the criteria for the diagnosis of dementia. In these cases the use of PET (Positron Emission Tomography) can be very effective.

PET provides metabolic information. PET scans are usually performed in association with others that provide anatomical imaging, such as magnetic resonance imaging (MRI) or computed tomography (CT), since the overlapping of data obtained by both techniques allows a better evaluation of the results. PET devices currently available on the market are hybrid systems and have a computerized tomography (CT) or magnetic resonance (MR) in their structure. Brain activity can be visualized by PET through regional cerebral blood flow (perfusion) imaging, metabolic mapping, and mapping of neuroreceptor binding through the use of radioactive molecules, called radiopharmaceuticals.

The radiopharmaceutical fludesoxyglucose [FDG (18F)] is an analogue of glucose and has the radioactive element fluoro 18 in its molecule. Because it is an analog of glucose, it concentrates in cells that use glucose as a source of energy or in cells whose glucose dependence is increased by pathophysiological changes.[1] The main substrate for cerebral metabolism is glucose and the cerebral metabolic rate is an important indicator for the evaluation of normal function and pathological alterations of this organ.[2] There is a small age-dependent reduction in the cerebral metabolic rate of global glucose and this change in the aging process may be related to the significant reduction of synapses, dendrites and myelinated fibers, which occur with the relative reduction of cortical neurons. These changes may partly justify cases of increased cognitive difficulties, cerebral atrophy and marked diffuse reduction of frontal metabolism.[3] Regional and global changes are important in assessing the severity of diseases as well as in the differential diagnosis of brain diseases.

In Alzheimer Disease (AD) changes in metabolic rates can occur up to 20-30 years before the onset of symptoms,[4] so PET/CT with FDG (18F) may be a valuable early diagnostic tool of AD. A significant reduction of the metabolic rate in the hippocampus was detected in normal individuals who progressed to AD, whereas cortical hypometabolism (prefrontal cortex, temporoparietal and posterior cingulate) was observed at the onset of symptoms.[5,6] Similarly, individuals with MCI or early stages of dementia also had this reduction in metabolic rate.[5,6] Other studies[7] have demonstrated the relationship of symptom severity and regional hypometabolism in patients with probable AD, whereas in healthy subjects FDG (18F) uptake significantly reduced with age in both the anterior cingulate and the cortex frontolateral. Unlike the neocortical association areas, there is the preservation of the basal ganglia, thalamus, cerebellum, sensorimotor cortex and visual cortex.[8,9]

While AD represents about 50% to 60% of all cases, Lewy Body Dementia (LBD) and frontotemporal dementia (FTD) account for 15 to 25%.[10] In these pathologies, the use of PET/CT with FDG (18F) can provide information on the progression of regional functional disorders related to the severity of cognitive and memory deficits, as well as to aid in the differential diagnosis. Hemodynamic asymmetry of glucose hypometabolism usually lateralizing to the left is a common feature in patients with FTD, which may aid in the differentiation of AD or other causes of dementia.[11,12]

PET/CT brain imaging with FDG also evidenced differentiation in hypometabolism patterns between AD and LBD patients. In patients with LBD, severe hypometabolism was observed in the occipital cortex, preserving the mesial portion of temporal lobes, contrasting with findings in patients with AD.[13]

These metabolic findings are also seen in patients with Parkinson's disease (PD) and PD with dementia, as they also share the same pathophysiology of LBD, due to the accumulation of Lewy Bodies in the cerebral cortex.[14]

Frontotemporal lobar degeneration (FTLD) is the second most common cause of dementia in individuals younger than 65 years and is clinically characterized by personality changes and cognitive disorders. Patients with FTLD present metabolic disorders mainly in the frontal lobes and temporal poles, with less pronounced involvement in the parietal lobes, which are affected only in the more advanced stages of the disease.[15] This pattern of predominantly frontal hypometabolism facilitates the differential diagnosis between AD and FTLD, although with some degree of overlap, since the frontal regions may be equally affected in AD, as well as involvement of the associative temporoparietal cortex can occur in FTLD.[16,17]

Also in PD the cerebral metabolic rate of glucose may aid in differential diagnosis. Hypometabolism was observed in the striatum in atypical parkinsonian syndrome, whereas in PD the metabolic rate is normal or elevated.[18] The different regional glucose metabolism patterns observed in PET/CT with FDG (18F) may aid in the differentiation of PD from other parkinsonian syndromes with 95% sensitivity and 94% specificity.[19]

In Brazil there are PET/CT operating in almost all major capital cities and the FDG (18F) is supplied daily to the Nuclear Medicine services of the main hospitals. It increases the chances of performing in vivo noninvasive brain studies, enabling early detection of metabolic abnormalities, monitoring of pharmacological therapies, and clinical staging. With the brazilian current demographic profile, the access to PET/CT is a major step towards qualifying public health services and its implementation at an appropriate scale is a major challenge for health managers.

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