BAOJ Neurology

Lakshmi Narasimhan Ranganathan,et al., BAOJ Neurol 2018, 4: 2

4: 056

Research

Pattern of Hypo Metabolism in FDG Pet in Alzheimers Disease: Experience from a Tertiary Care Centre

Lakshmi Narasimhan Ranganathan[1*], AV Srinivasan[2], Suriyakumar G[3], Srinivasaraman G[3], Thamil Pavai N[4], Guhan R[5], Keerthana V[6] and Arun Shivaraman MM[5]

[1]Director and Professor, Institute of Neurology, Madras Medical College, Chennai

[2]Emeritus Professor, the Tamil Nadu Dr. MGR Medical University, Chennai

[3]Consultant Radiologist, Anderson Diagnostics and Labs, Chennai,

[4]Associate Professor, Institute of Neurology, Madras Medical College, Chennai,

[5]Resident, Institute of Neurology, Madras Medical College, Chennai

[6]Research Assistant, Anderson Diagnostics and Labs, Chennai

Introduction

The prevalence of dementia is increasing with the increasing longevity of the population. The prevalence of dementia is estimated to be 66 million by 2030 [1]. It affects the cognitive domains including attention, memory, language, social cognition, perceptual motor and executive function that interferes with the quality of living [2]. Clinical approach to dementia forms the basis of diagnosis in routine clinical practice. However with the emergence of disease modifying therapies in the management of patient with dementia, the use of diagnostic studies to diagnose in the preclinical phase and aid in the clinical diagnosis during situations of dilemma is of paramount importance. The cause of dementia may be either primary or secondary. Alzheimers Disease is the most common cause of primary dementia in the world. The prevalence of Alzheimer disease worldwide is 35.6 million in 2009 and it results in significant economic burden to the individual and the community [3]. Alzheimer's disease is pathologically characterized by accumulation of beta amyloid plaque and neurofibrillary tangles. It progressively impairs memory and other cognitive domains. Variants of Alzheimer's disease with similar pathology include posterior cortical atrophy, logopenic variant of Primary progressive aphasia [4].

The use of imaging in aiding the diagnosis of Alzheimer's disease has evolved over the years and has paralleled the development of CSF biomarkers. However, owing to the non invasiveness and availability of the imaging modality, it is widely being used across the world. Imaging studies are categorised as structural, functional and molecular imaging. Structural imaging includes conventional magnetic resonance imaging, voxel based morphometric analysis and diffusion tensor imaging. Functional imaging includes 18F-Fluorodeoxyglucose Positron Emission Tomography (FDG PET) and functional MRI. Molecular imaging includes amyloid imaging (radiolabelled tracers bind to beta amyloid plaque) and tau imaging (radiolabelled tracers bind to neurofibrillary tangles). The FDG PET utilises 18F - labelled tracer bound to glucose and helps assess the hypo metabolism in the brain. The use of FDG PET in dementia has seen a rapid rise. The pattern of hypometabolism in FDG PET aids in the diagnosis of Alzheimer's disease, but cannot be used as an independent modality to establish the diagnosis. In our institute and tertiary care hospital we aim to analyse the pattern of hypo metabolism in Alzheimers disease [5].

***Corresponding Author:** Lakshmi Narasimhan Ranganathan, Director and Professor, Institute of Neurology, Madras Medical College, Chennai, E-mail: lakshmineuro@gmail.com

Sub Date: June 12th 2018, **Acc Date**: June 18th 2018, **Pub Date**: June 19th 2018.

Citation: Lakshmi Narasimhan Ranganathan, AV Srinivasan, Suriyakumar G, Srinivasaraman G, Thamil Pavai N, Guhan R, Keerthana V and Arun Shivaraman MM (2018) Pattern of Hypo Metabolism in FDG Pet in Alzheimers Disease: Experience from a Tertiary Care Centre. BAOJ Neurol 4: 56.

Material and Methods

Patients attending our Cognitive Neurosciences and Dementia clinic in the institute of Neurology, Rajiv Gandhi Government General Hospital were recruited. A probable diagnosis of Alzheimer's dementia was considered based on the criteria established by the National Institute on Aging and the Alzheimer's Association (NIA-AA). Battery of Neuropsychological tests were performed including Montreal cognitive assessment (MoCA), Addenbrooke's Cognitive Examination (ACE-III). The patients were subsequently subjected to FDG PET imaging.

Preparation of the patient for FDG PET was carried out and it included maintaining a blood glucose level of less than 140 mg/dl and avoiding dextrose containing fluid as it shall interfere with imaging. Drugs such as benzodiazepines, barbiturates were avoided. If sedation were required for patients, benzodiazepines were administered 30 minutes after the administration of the radioactive tracer prior to the FDG PET imaging. The consumption of alcohol, caffeine, nicotine and tea were avoided before the procedure. The patient was advised to be in a wakeful state with eyes open to avoid artifactual hypo metabolism in the occipital cortex.

Then image acquisition and processing is as follows. A dose of about 3 Mbq/kg of the radioactive tracer 18 F-Fluorodeoxyglucose is administered. FDG PET imagines performed 30 minutes after the administration of the radioactive tracer. The acquired image is analysed, processed and projected onto a standard templates comparable to the standard Thalaiarch atlas. The processed image is matched to the corresponding voxel in the template. The resultant gray scale image is colour coded based on the Z scores that are mapped onto the template. Z score is derived in comparison to the reference set of data derived from global normalisation. A positive Z score indicates hypo metabolism and a negative Z score indicates hyper metabolism. Using 3D stereotactic surface projection, the images are projected and analysed. Corresponding Computed tomography imaging of the brain is done for comparison with functional counterpart.

The Z scores were compiled and the region of hypo metabolism were documented. Descriptive analysis of the compiled data was performed.

Results

A total of 6 patients were analysed as a part of the study. 3 patients were females and 3 patients were males, Figure 1. 3 patients were illiterate and did not receive any formal education. All the patients were right handed. The highest educational qualification in the above cohort was tenth standard.

The pattern of hypo metabolism noted are as follows. Hypometabolism in the right and left parietal association cortex was observed in 5 patients. Hypometabolism in the right and left temporal association cortex was noted in 6 and 5 patients respectively. in the right and left frontal association cortex, hypo metabolism was noted in 4 and 3 patients respectively. In right and left occipital association cortex, hypometabolism was noted in 4 patients. However, hypo metabolism in the visual cortex was noted in only 3 patients on the left side and 2 patients on the right side. Hypometabolism in the right and left posterior cingulate cortex was noted in the 4 patients. Hypometabolism in the right and left anterior cingulate cortex was noted in 5 and 4 patients respectively. Hypometabolism in right and left medial frontal cortex was noted in 2 patients. Hypometabolism in right and left medial parietal cortex was noted in 4 patients and 4 patients respectively. Hypometabolism in caudate nucleus was observed in all 6 patients on either sides. Figure 2.

The analysis of areas with hypo metabolism of Z score beyond 2 revealed the following. Z score beyond 2 was noted in right and left parietal association cortex in 3 patients, right and left frontal association cortex in 1 patient, right occipital association cortex in one patient and left occipital association cortex in another, right and left temporal association cortex in 1 patient and 2 patients respectively, right and left posterior cingulate cortex in 2 patients, in left medial parietal cortex in 3 patients, in left and right caudate nucleus in 1 patient. Figure 3. One such typical pattern is depicted in Figure 4.

Discussion

Alzheimer's disease is characterised by accumulation of beta amyloid and neurofibrillary tangles resulting in neuronal dysfunction. The neuronal dysfunction is elucidated using FDG PET imaging and is visualised as hypo metabolism. The signature pattern of cortical involvement is evidenced as specific pattern in the FDG PET. The pattern of involvement noted in the early stages of Alzheimer's disease include parietal association cortex, temporal association cortex, posterior cingulate cortex. The involvement of posterior cingulate cortex is more specific for Alzheimer's disease. However, involvement of parietal and temporal association cortex is highly sensitive for Alzheimer's disease. As the disease advances in frontal association cortex are involved. Anterior cingulate cortex and primary sensorimotor cortex are usually spared [6]

The above mentioned pattern of hypo metabolism is visualised in the descriptive analytical process that considers Z score beyond 2. The parietal association cortex and posterior cingulate gyrus are more commonly involved followed by involvement of temporal association cortex, frontal association cortex, and medial parietal cortex as the disease advances. Primary sensorimotor cortex is spared in the disease process. Similarly, sparing of the occipital cortex is evident and it helps differentiate from dementia with levy bodies. However, Posterior cortical atrophy variant of the Alzheimer's disease may present with hypo metabolism of the visual and visual association cortices.

The involvement of caudate nucleus is unusual and is more commonly found in other causes of dementia such as behavioural variant of front temporal dementia and corticobasal degeneration. However similar

findings of caudate involvement have been reported in volumetric analysis. In autopsy studies in patients with Alzheimer's disease, pathological changes in caudate nucleus have been noted. However, its role in the clinical symptomatology in Alzheimer's disease requires further attention [7,8].

FDG PET is also useful in predicting the progression of Minimal cognitive impairment to Alzheimer's disease. The involvement of medial temporal cortex in the screening of patients with amnestic MCI is predictive of conversion to Alzheimer's disease. The FDG PET has a high sensitivity and specificity compared to other imaging and CSF modalities used in the investigation of patients with dementia. The elucidation of the pattern of hypo metabolism and the identification of primary dementia can help institute therapy in these patients early in the course of the disease. Limitations of the study include small sample size. The use of FDG PET with MR fusion may improve spatial localization [9].

Conclusion and Limitations

The increasing wide spread use of FDG PET in elucidating the ethology is of utmost importance. Z scores are invaluable markers of hypo/hyper metabolism and its importance is highlighted here to understand the signature pattern of uptake in AD. The pattern of hypo metabolism observed is useful for differentiating AD from other types of dementia. In Alzheimers disease the pattern of hypo metabolism includes involvement of parietal association cortex, temporal association cortex, posterior cingulate cortex, medial parietal cortex. Involvement of frontal association cortex and anterior cingulate cortex is noted in the later stages of the disease. There was relative sparing of the sensor motor cortex and occipital cortex. Moderate hypo metabolism of the caudate was noted which requires further elucidation. The uniqueness of this study is comparison of the Z scores of hypometabolism among various anatomical areas. The limitations of this antemortem study are that the sample size is small and hence clinico-PET concordance could not be ascertained.

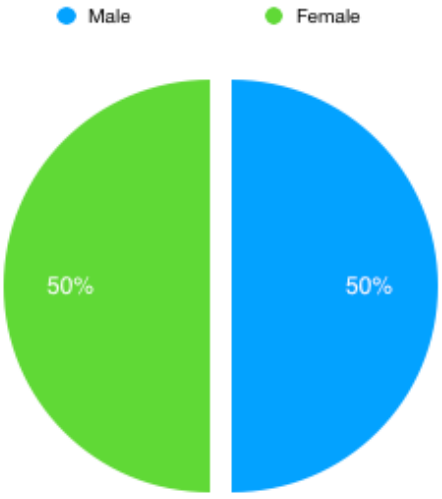

Figure 1. Gender distribution in the studied subjects

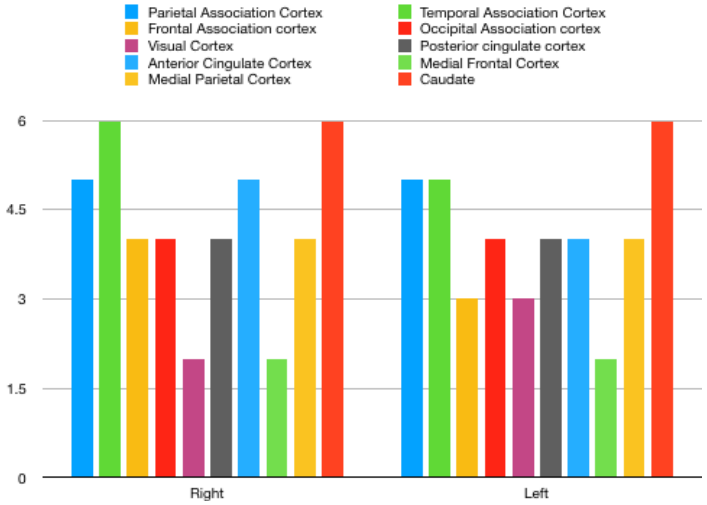

Figure 2. Hypometabolism (positive Z score) visualised in the studied subjects in various lobes.

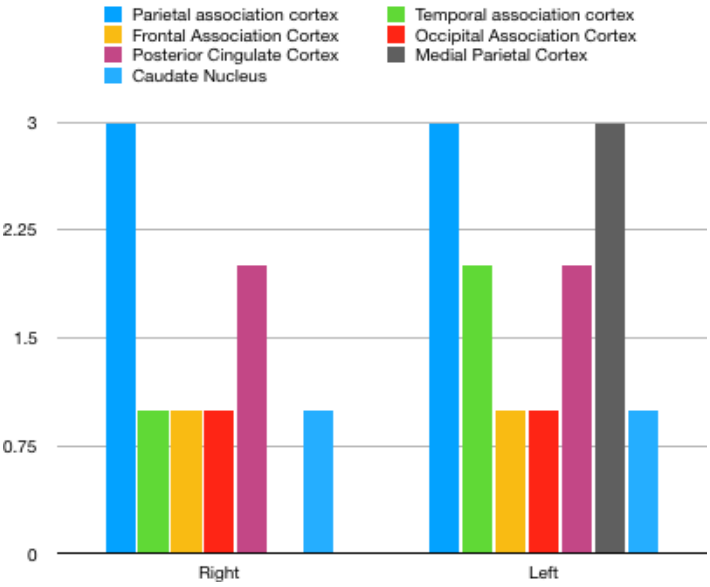

Figure 3. Hypometabolism with a Z score of >2 in the studied subjects in various lobes.

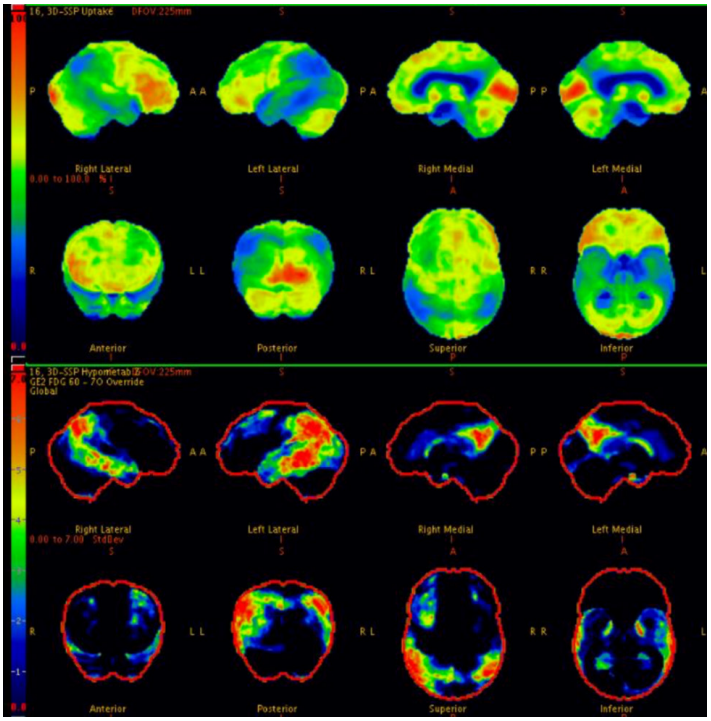

Figure 4. Alzheimer's disease. Severe hypo metabolism is noted in bilateral parietal and temporal cortices. Moderate hypo metabolism is noted in bilateral frontal lobes.

References

1. Wortmann M (2012) Dementia: a global health priority— highlights from an ADI and World Health Organi- zation report. Alzheimers Res Ther 4(5): 40.
2. Knopman DS, DeKosky ST, Cummings JL (2001) Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 56(9): 1143-1153.
3. Prince M, Ferri CP, Sousa R (2014) World Alzheimer report 2009.
4. Masliah E, Mallory M, Deerinck T (1993) Re-evaluation of the structural organization of neuritic plaques in Alzheimer's disease. J Neuropathol Exp Neurol 52(6): 619-632.
5. Rayment D, Biju M, Zheng R, Kuruvilla T (2016) Neuroimaging in dementia: an update for the general clinician. Progress in Neurology and Psychiatry 20(2): 16-20.
6. Brown RK, Bohnen NI, Wong KK, Minoshima S, Frey KA (2014) Brain PET in suspected dementia: patterns of altered FDG metabolism. Radiographics 34(3): 684-701.
7. Rombouts SA, Barkhof F, Witter MP, Scheltens P (2000) Unbiased whole-brain analysis of gray matter loss in Alzheimer's disease. Neuroscience letters 285(3): 231-233.
8. Braak H, Braak E (1990) Alzheimer's disease: striatal amyloid deposits and neurofibrillary changes. Journal of Neuropathology & Experimental Neurology 49(3): 215-224.
9. Shivamurthy VK, Tahari AK, Marcus C, Subramaniam RM (2015) Brain FDG PET and the diagnosis of dementia. American Journal of Roentgenology 204(1): W76-85.