

# Comparison of Visual Rating Scale Based on Brain 18F-FDG-PET and Montreal Cognitive Assessment Test in Probable Alzheimer's Disease

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## ABSTRACT

**Objectives:** Recently, imaging biomarkers like fluoro-deoxy-glucose positron emission tomography (FDG-PET) become even more important for evaluation probable AD. The aim of this study was to evaluate the possible correlation between Montreal Cognitive Assessment Test (MoCA) and metabolic function of brain regions determined by FDG-PET in patients with probable AD.

**Materials and methods:** Thirty seven (37) patients who had diagnosis of probable AD were included. MoCA test and metabolic measurements of brain regions by FDG-PET were performed in all patients. A visual scoring was performed to obtain the rates of hypometabolism in brain regions.

**Results:** Median age of the patients was 77 (minimum 65-maximum 83) years. On the right hemisphere, MOCA test score decreased according to visual FDG-PET score of parietal lobe ( $15\pm 5.1$ ,  $11.8\pm 8.4$  and  $8.5\pm 5.9$ ;  $p=0.032$ ). MOCA test score was  $16\pm 5.8$ ,  $13.1\pm 7.6$  and  $9.1\pm 6.1$  in patients with left temporal lobe and  $15.2\pm 5.2$ ,  $11.8\pm 7.8$  and  $8.5\pm 5.9$  in patients with left parietal lobe according to visual FDG-PET scores respectively ( $p=0.035$ ;  $p=0.02$ ). The comparison of the other right and left hemisphere regions and MOCA test scores were not significant.

**Conclusion:** The present study is emphasized that the MoCA test which is easily applied in outpatient clinics can be demonstrated the hypometabolism of bilateral parietal and left temporal brain regions related with pathophysiology of AD.

**Keywords:** Fluoro-deoxy-glucose positron emission tomography, hypometabolism, montreal cognitive assessment test, Alzheimer disease

Received: 14 February 2022, Accepted: 4 April 2022,  
Published online: 13 June 2022

## INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disease and the most common cause for dementia [1]. Cognitive impairment related to AD is a progressive condition and the diagnosis is based on clinical evaluation along with brain imaging. Magnetic resonance imaging (MRI) is the modality of choice to exclude non-alzheimer diseases. Additionally, the pattern and extent of brain atrophy on structural MRI scans can be used to support the diagnosis of AD [2]. The degree of brain atrophy can also be demonstrated by MR volumetric measurement but not routinely used because of its detailed and inconvenient nature [3]. Brain flor-18 fluoro-deoxy-glucose (FDG)-positron emission tomography (PET), which has long been frequently used in the diagnosis of neurodegenerative diseases, is deemed as the viable method for in-vivo examination of regional human brain metabolism in healthy human or disease state [4,5].

The Montreal Cognitive Assessment (MoCA) is one of the most common screening instruments developed in 2005. Using a cut-off score of 26 or above provides sensitivity and specificity for excluding normal conditions of 90% and 87%, respectively [6]. Although the MOCA cognitive screening tool has widely used in clinical practice, there are limited data on metabolic function in brain regions associated with MoCA score. The aim of this study was to analyze the relationship between MoCA tests and brain FDG-PET imaging of the patients, who are clinically considered to have AD, the most frequent etiologic cause of dementia.

## MATERIALS AND METHODS

### Study Population and Neuropsychiatric Assessment

This cross-sectional study was performed with 37 probable AD patients aged over 65 years admitted to the geriatric outpatient clinic of our center. All patients underwent MoCA test and FDG-PET imaging. Brain MRI was performed for all patients to exclude other causes of dementia. MoCA tests were administered to all patients routinely according to

the standard instructions. [6-8]. The test consists of 13 tasks organized into eight cognitive and thinking domains including Visuospatial/Executive Function, Animal naming, Clock-drawing test, Attention, Language, Abstraction, Short-term memory, and Orientation. A total score ranges from 0 to 30. The MoCA score was considered abnormal if less than 26 [9].

Written informed consent was obtained from all participants. The study was ethically approved by the Hacettepe University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (16969557-No. 12 and Decision No. GO 15/763-13).

### Brain FDG-PET imaging

8 mCi 18F-FDG was administered intravenously when fasting blood glucose levels were within normal values following 12 hours of fasting. Sixty minutes after injection, images in three-dimensional mode were taken from the vertex till upper mediastinum. Axial, coronal and sagittal slices were obtained after making attenuation correction with CT on the images obtained. The slices obtained were assessed visually and using SPM analysis.

The PET images of patients which were present in the PACS system were reevaluated by four specialists working in the Nuclear Medicine Department. A visual scoring was performed between 0 and 2 in order to obtain the rates of hypometabolism in brain regions. (0: normal metabolism, 1: mild hypometabolism, 2: moderate-severe hypometabolism).

### Statistical Analysis

Statistical evaluation was performed using Statistical Package for Social Sciences 20 (SPSS) for Windows (IBM SPSS Inc., Chicago, IL) program. The variables were investigating using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov / Shapiro-Wilk's test) to determine whether or not they are normally distributed. Variables with normal distribution were shown as mean  $\pm$  standard deviation while those without normal distribution were shown as median

with minimum and maximum range. Categorical variables were shown as number and percentage. As the MoCA scores were normally distributed the one-way ANOVA tests were conducted to compare this parameter and visual FDG-PET scores. Levene test was used to assess the homogeneity of the variances. When an overall significance was observed, pairwise post-hoc tests were performed using Tukey's test.  $p \leq 0.05$  values were accepted as significant in the intergroup comparison results.

## RESULTS

### Baseline Demographic Characteristics

Of 37 patients, 20 were (54.1%) male and 17 (45.9%) were female. The median age was 77 years (minimum 65 – maximum 83). In whole population, the rates of comorbidities were as follows; diabetes mellitus (DM) 21.6%, hypertension (HT) 40.5%, coronary artery disease (CAD) 40.5%, thyroid dysfunction 27.0%, osteoporosis 27.0%, asthma/chronic obstructive pulmonary disease (COPD) 5.4% and urinary incontinence 29.7%. Median MoCA test score was 12 (minimum 1 – maximum 24). Median education years of the patients were 8 years (minimum 5- maximum 21)

### Metabolic Assessment Results

The results of metabolic assessment via FDG-PET in different brain regions are presented in Table 1. The left temporal lobe was found to be the most common site of moderate to severe hypometabolism observed in 16 of 37 patients

**Table 1.** Metabolic assessment of different brain regions with FDG PET

	Visual Score of Hypometabolism		
	Score 0 n (%)	Score 1 n (%)	Score 2 n (%)
<b>Right frontal</b>	28 (75,7)	0 (0)	9 (24,3)
<b>Left frontal</b>	25 (67,6)	3 (8,1)	9 (24,3)
<b>Right temporal</b>	16 (43,2)	7 (18,9)	14 (37,8)
<b>Left temporal</b>	15 (40,5)	6 (16,2)	16 (43,2)
<b>Right parietal</b>	17 (45,9)	8 (21,6)	12 (32,4)
<b>Left parietal</b>	16 (43,2)	9 (24,3)	12 (32,4)
<b>Right precuneus</b>	24 (64,9)	7 (18,9)	6 (16,2)
<b>Left precuneus</b>	23 (62,2)	6 (16,2)	8 (21,6)

(43.2%) and followed by the right temporal lobe with 37.8% and left and right parietal lobes with 32.4%. On the other hand, the most common region of normal metabolic activity was noted in the right frontal region with 75.7%. The least common sites of normal metabolic activity were the left and right temporal lobes (40.5% and 43.2%, respectively).

### MoCA and visual FDG-PET scores

The comparison of visual FDG-PET scores and MoCA test results are presented in Table 2. Hypometabolism of right hemisphere regions were not associated the MoCA score except right parietal lob. Mean MoCA test score was  $15 \pm 5.1$ ,  $11.8 \pm 8.4$ , and  $8.5 \pm 5.9$  according to visual FDG-PET score of 0, 1, and 2 in the right parietal region. The difference was statistically significant ( $p=0.032$ ).

**Table 2.** Comparison of visual FDG-PET scores and MoCA test results

	Right Hemisphere		Left Hemisphere	
	MoCA Mean ( $\pm$ SD)	p	MoCA Mean ( $\pm$ SD)	p
<b>Parietal</b>		<b>0.032</b>		<b>0.02</b>
Score 0	15.0 ( $\pm 5.1$ )		15.2 ( $\pm 5.2$ )	
Score 1	11.8 ( $\pm 8.4$ )		11.8 ( $\pm 7.8$ )	
Score 2	8.5 ( $\pm 5.9$ )		8.5 ( $\pm 5.9$ )	
<b>Temporal</b>		0.09		<b>0.035</b>
Score 0	13.7 ( $\pm 5.8$ )		16 ( $\pm 5.8$ )	
Score 1	14.8 ( $\pm 7.9$ )		13.1 ( $\pm 7.6$ )	
Score 2	9.2 ( $\pm 6.3$ )		9.1 ( $\pm 6.1$ )	
<b>Frontal</b>		0.13		0.19
Score 0	13.2 ( $\pm 7$ )		12.8 ( $\pm 7.1$ )	
Score 1	-		16.6 ( $\pm 6.4$ )	
Score 2	9.3 ( $\pm 4.3$ )		9.3 ( $\pm 4.3$ )	
<b>Precuneal</b>		0.26		0.40
Score 0	13.3 ( $\pm 6.2$ )		13.4 ( $\pm 6.3$ )	
Score 1	11.2 ( $\pm 9.1$ )		10.5 ( $\pm 7.5$ )	
Score 2	9 ( $\pm 4.8$ )		10.2 ( $\pm 7.1$ )	

The mean MoCA score of the patients with moderate to severe visual score of left parietal and left temporal lobe hypometabolism was lower than the other patients. MoCA test score was  $16 \pm 5.8$ ,  $13.1 \pm 7.6$ , and  $9.1 \pm 6.1$  in patients with left temporal lobe visual score 0, 1, and 2, respectively ( $p=0.035$ ).

In patients with left parietal lob visual FDG-PET score 0, 1, and 2, mean MoCA score was  $15.2 \pm 5.2$ ,  $11.8 \pm 7.8$ , and  $8.5 \pm 5.9$  ( $p=0.02$ ) (Figure 1). The comparison of the other left hemisphere regions and MoCA test scores were not significant.

## DISCUSSION

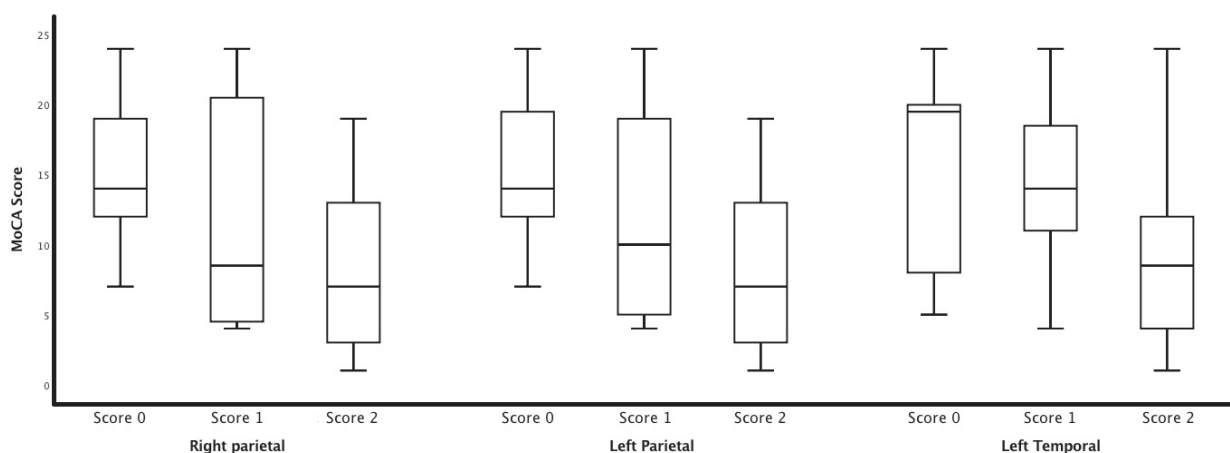
In this study, we have systematically investigated the relationship between cognitive performance status and brain glucose metabolism in probable AD patients. Regional glucose hypometabolism has been able to demonstrate highest percentage of variance in the MoCA test scores. This is the first study using visual FDG-PET score to demonstrate the impairment in MoCA performance in patients with probable AD.

There are many methods to evaluate the cognitive impairment of patients in geriatric outpatient clinics. MoCA test is a common screening tool used in cognitive function assessment. The test assesses additionally attention, concentration, working memory, and language [8]. Recently, brain FDG-PET imaging methods have been introduced in clinical and research practice to diagnose of Alzheimer disease [4,5]. A meta-analysis including 27 different studies performed on patients with AD has shown that the sensitivity and specificity of FDG-PET were 91% (confidence interval 86 – 94%) and 86% (confidence interval 79 – 91%), respectively [10]. A pattern of hypometabolism is typically observed in the parietal, temporal and the posterior cingulate cortex regions in the AD [5,11]. Many researchers have shown that the diagnostic sensitivity of

hypometabolism in the temporoparietal cortical areas varies; it is approximately 90% for patients with AD [12]. In our study, incidence of hypometabolism was ranked as temporal, parietal, precuneal and frontal similar with literature. When the disease progressed, the frontal lobe might also be affected. Our patients did not have frontal hypometabolism that might be related early phase of Alzheimer.

A few studies have been published searching correlation between geriatric assessment tests and brain FDG metabolism. In a study, decreased  $^{18}F$  – FDG uptake in the left and right precuneus, left fusiform gyrus, and left middle orbitofrontal gyrus have shown trend toward to with decreased MoCA score but significant correlation was shown only left posterior cingulate gyrus, an AD signature area ( $p=0.007$ ) [13]. In another recently published study performed on 27 AD patients, the range of reduced FDG metabolism was negatively correlated with the total scores of MoCA. In the detailed brain region analyses, significant correlation was shown between reduced FDG metabolism of left parietotemporal and MoCA score ( $p=0.04$ ) [14]. Similarly in our study MoCA test score did not differ according to visual score of frontal and precuneal hypometabolism. Median MoCA score significant decreased in patient with high left parietotemporal hypometabolism score. Unlike these studies, we have used a visual score including 3 categories to obtain the rates of hypometabolism.

Some study was performed to explain the relationship between domains of MoCA test and functional brain imaging. Clock drawing test (CDT) is a pair of MoCA test requires intact visuoconstructive skills which are mainly represented in the



**Figure 1.** Box plots showing the median Montreal Cognitive Assessment (MoCA) score by visual FDG-PET score of brain regions where were found statistically significant.

parietal lobe. In a study included 71 patients, positive correlation between CDT scores and parietal glucose metabolism in the AD patients ( $z$  score=3.68;  $p<0.001$ ) [15]. Another domain of MoCA test is calculation which is required the linguistic representation and visuospatial imaginary was evaluated on 91 patients. Arithmetic test score of the patients and FDG-PET glucose metabolism showed significant correlation with in the left inferior parietal lobe ( $r=0.405$ ,  $p<0.0001$ ) and in the left inferior temporal gyrus ( $r=0.381$ ,  $p=0.0002$ ). Abstraction domain of MoCA test requires semantic knowledge and conceptual thinking. On a PET imaging study showed that the metabolic reduction in the left temporal lobe correlates with impairment of abstraction function [16]. In our study, although the subdomains of the MoCA test were not examined individually, a correlation between MoCA scores and hypometabolism of parietal and temporal lobes was demonstrated in parallel with the literature.

This study is one of the study showing that a complex and inaccessible biomarker such as PET-CT mediated metabolic imaging can yield correlated results with MoCA that are easily applied and reproducible in the outpatient clinic.

## CONCLUSION

Along with the ever-increasing elder population, the fact that dementia and AD will be encountered more frequently, leads to the renovation and elaboration of the tests to be used in the diagnostic

process. Our results emphasize the relationships between brain glucose hypometabolism in patients with AD and their impact on cognitive functioning or vice versa. However, there is a need for prospective studies with larger number of patients and in which the measurements are repeated over time and compared with the baseline values.

## Author contribution

Study conception and design: EA and MH; data collection: EA, PD, and EB; analysis and interpretation of results: KKO, BVS, BE, and ELE; draft manuscript preparation: BBY, MC, and MH. All authors reviewed the results and approved the final version of the manuscript.

## Informed consent

Written informed consent was obtained from all participants.

## Ethical approval

The study was approved by the Hacettepe University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (16969557-No. 12 and Decision No. GO 15/763-13, 06/01/2016).

## Funding

The authors declare that the study received no funding.

## Conflict of interest

The authors declare that there is no conflict of interest.

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