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The value of FDG-PET/CT by using 3-dimensional stereotactic surface projection software analysis in the differential diagnosis of dementia

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Background/aim: To retrospectively reevaluate brain fluor-18-fluorodeoxyglucose positron emission tomography (FDG-PET) imaging studies with 3-dimensional stereotactic surface projection (NEUROSTAT) software in order to detect changes in regional brain metabolism and to find out its contribution to the final diagnosis.

Materials and methods: A total of 48 cases were included in this study. According to clinical evaluation and neuropsychometric test results, there were 17 (35%) patients with probable Alzheimer disease (AD), 17 (35%) patients with probable frontotemporal dementia (FTD), and 14 (30%) patients with undefined advanced dementia. Brain FDG-PET imaging studies were interpreted visually and also using 3-dimensional stereotactic surface projection.

Results: Clinic and PET findings were consistent in 20 patients and inconsistent in 14 patients. When consensus diagnosis was taken as the reference, the sensitivity, specificity, accuracy, and positive and negative predictive values of FDG-PET imaging were 93%, 85%, 90%, 90%, and 89% respectively, for AD diagnosis. The same values were 85%, 93%, 90%, 89%, and 90%, respectively, for FTD definition.

Conclusion: Using automatized programs that enable quantitative evaluation of regional brain glucose metabolism, in addition to visual evaluation, may increase diagnostic efficiency, as well as minimize interobserver and/or intercenter variability.

Key words: Alzheimer disease, frontotemporal dementia, fluor-18-FDG-PET, brain positron emission tomography

1. Introduction

Diagnosing and differentiating dementia is becoming increasingly important, as there are several new disease-specific and effective treatment options. However, the only way to definitively diagnose dementia is with a postmortem histopathological examination. Therefore, patients are currently diagnosed with a "probable cause" of dementia and treated for symptoms based on clinical history, progress and variation of symptoms, laboratory tests, brain scans, and neuropsychological assessments. These diagnostic tests are highly accurate in advanced dementia cases, but even in the most experienced clinics, patients in the early stages of dementia may be misdiagnosed if the symptomatology of the disease is not yet present (1). Therefore, there is a need for a technique that can be used to determine a reliable diagnosis of dementia that can also identify the pathognomonic changes of the early stages of disease.

Fluor-18-fluorodeoxyglucose positron emission tomography (FDG-PET) can detect glucose consumption in vivo. This technique can be used to determine the difference in glucose metabolism in the early phases of pathophysiological processes, before these differences cause morphological changes. FDG-PET can detect areas with reduced glucose consumption, including neurodegeneration and gliosis in the central nervous system. Therefore, this method can also be used to diagnose other neuropsychiatric processes (2).

Many studies have shown that FDG-PET imaging can detect different topographical distributions of regional brain glucose metabolism and therefore can aid in the various diagnoses of dementia, including Alzheimer disease (AD), frontotemporal dementia (FTD), vascular dementia (VD), and dementia with Lewy bodies (DLB) (3,4). In cases of AD, a pattern of hypometabolism is typically observed in the parietotemporal cortex and

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in the posterior cingulate cortex regions. In addition to those regions affected in AD cases, areas of the visual cortexes are also affected in DLB cases. However, in cases of FTD, lower FDG uptake is first observed in the frontal lobes and in the anterior temporal regions. In VD cases, multiple focal hypometabolic areas are generally observed, which indicates a random distribution in the cerebral cortex. Many researchers have shown that the diagnostic sensitivity of hypometabolism in the temporoparietal cortical areas varies; it is approximately 90% for patients with AD (5–7). On the other hand, some researchers have shown that the diagnostic accuracy of FDG-PET is lower than 90%, especially in the early stages of the disease (8–10). The diagnostic accuracy of FDG-PET can be increased if the images are evaluated by an experienced physician and/or if the images are evaluated with software capable of conducting quantitative statistical analyses, such as 3-dimensional stereotactic surface projection (3D-SSP) and statistical parametric mapping (SPM). These programs can be used to increase the diagnostic accuracy of FDG-PET by decreasing the number of false positive or false negative results in the early stages of the disease, or in cases with atypical clinical presentations (11,12).

The aim of this study was to determine the importance of FDG-PET imaging for the diagnosis of dementia in patients with an early diagnosis of dementia in accordance with the National Institute of Neurologic and Communicative Disorders and Stroke (NINCDS) and Alzheimer's Disease and Related Disorders Association (ADRDA) criteria. All PET images were reevaluated retrospectively with 3D-SSP NEUROSTAT software to compare changes in regional brain metabolism. In addition, data derived from neuropsychological tests were also taken into consideration.

2. Materials and methods

2.1. Patients

After obtaining approval from the ethics committee, this study included 48 patients who underwent neuropsychometric tests and brain FDG-PET imaging between December 2005 and April 2011. The data were examined retrospectively with the aim of obtaining the differential diagnosis of dementia. All of the patients had a probable diagnosis of dementia based on criteria developed by NINCDS-ADRDA and/or frontotemporal lobar degeneration. The mean age of the patients was 61.48 ± 8.60 years (range: 29–81 years), and 14 of the patients (29%) were male and 34 were female (71%). Table 1 summarizes the mean age, years of education, and sex distribution of the patients. According to the clinical findings and neuropsychological test results (CLINIC), there were 17 (35%) patients with probable AD, 17 (35%) patients with probable FTD, and 14 (30%) patients with an undefined advanced dementia (Table 2).

2.2. Neuropsychological tests

The following tests were used to assess neuropsychological performance: Wechsler Memory Scale (WMS) subtest II, WMS subtest III, WMS subtest IV, WMS subtest VI, Wisconsin Card Sorting Test, Stroop Test, Binary Thinking and Analogies Test Abstraction, Boston Denotation, and Standardized Mini Mental Test.

2.3. ^{18}F-FDG PET/CT imaging

2.3.1. Image recording and processing

Following an intravenous injection of 259-518 MBq F-18 FDG, attenuation-corrected PET/CT (Siemens Biograph LSO HI-RES PET-CT, USA) images were acquired. After iterative reconstruction, 0.3-cm-thick section images from both CT and PET were obtained in the transaxial, coronal, and sagittal planes.

Table 1. The demographic characteristics of patients with the probable diagnosis of dementia.

Disease		Age, years	Education, years	Duration of disease, years	Female/male ratio (%)
AD	17	59.58 ± 6.91 (51–76)	8.64 ± 3.60 (5–15)	2.35 ± 0.8 (1–4)	13/17 (76)
Early stage	3	69.33 ± 7.02 (62–76)	7 ± 3.46 (5–11)	2.5 ± 0.7 (2–3.5)	1/3 (33)
Moderate stage	11	56.90 ± 4.45 (51–68)	9.18 ± 3.25 (5–15)	2.7 ± 0.87 (1–4)	9/11 (81)
Late stage	3	59.66 ± 7.23 (55–68)	8.33 ± 5.77 (5–15)	2.66 ± 0.76 (2–3.5)	3/3 (100)
FTD	17	62.29 ± 10.62 (29–80)	8.52 ± 4.09 (5–15)	2.66 ± 1.18 (0.25–5)	12/17 (71)
Early stage	6	65.16 ± 5.63 (59–75)	9.33 ± 4.96 (5–15)	2.75 ± 0.9 (1–4)	3/6 (50)
Moderate stage	8	59.75 ± 14.43 (29–80)	7.25 ± 3.70 (5–11)	2.53 ± 1.52 (0.25–5)	7/8 (87)
Late stage	3	63.33 ± 6.50 (57–70)	10.33 ± 5.03 (5–15)	2.83 ± 0.76 (2–3.5)	2/3 (66)
Undefined group	14	61.4 ± 11.58 (53–81)	5.57 ± 3.22(0–11)	2.57 ± 1.14 (1–4)	9/14 (64)

Table 2. Demographic and diagnostic characteristics of the patients.

No..	Name	Age/sex	Time (years)	Clinical diagnosis	PET diagnosis	Consensus diagnosis
1	MD	62/M	2	AD-EARLY STAGE	AD	AD-EARLY STAGE
2	AGK	70/M	2	AD-EARLY STAGE	FTD	AD-EARLY STAGE
3	KÇ	76/F	3.5	AD-EARLY STAGE	FTD	FTD-EARLY STAGE
4	GSA	55/F	1	AD-MODERATE STAGE	AD	AD-MODERATE STAGE
5	GA	57/F	3	AD-MODERATE STAGE	AD	AD-MODERATE STAGE
6	LÖ	60/F	2.5	AD-MODERATE STAGE	AD	AD-MODERATE STAGE
7	YK	57/F	2	AD-MODERATE STAGE	AD	AD-MODERATE STAGE
8	SA	54/F	3	AD-MODERATE STAGE	AD	AD-MODERATE STAGE
9	FB	58/F	4	AD-MODERATE STAGE	AD	AD-MODERATE STAGE
10	RC	54/F	3	AD-MODERATE STAGE	AD	AD-MODERATE STAGE
11	**ŞS**	58/F	2	AD-MODERATE STAGE	AD	AD-MODERATE STAGE
12	EM	51/F	2.5	AD-MODERATE STAGE	FTD	FTD-MODERATE STAGE
13	AE	68/M	4	AD-MODERATE STAGE	FTD	FTD-EARLY STAGE
14	MD	54/M	3	AD-MODERATE STAGE	FTD	AD-MODERATE STAGE
15	ZK	56/F	2.5	AD-LATE STAGE	AD	AD-LATE STAGE
16	ODU	68/F	3.5	AD-LATE STAGE	AD	AD-LATE STAGE
17	AD	55/F	2	AD-LATE STAGE	AD	AD-LATE STAGE
18	SE	68/F	4	UNDEFINED	AD	AD-LATE STAGE
19	ÜG	57/F	2.5	UNDEFINED	AD	AD-LATE STAGE
20	HŞ	81/M	2	UNDEFINED	AD	AD-LATE STAGE
21	AÖ	68/M	1	UNDEFINED	AD	AD-LATE STAGE
22	FÖ	59/F	4	UNDEFINED	AD	AD-LATE STAGE
23	NA	53/F	4	UNDEFINED	AD	AD-LATE STAGE
24	KÇ	67/F	2.5	UNDEFINED	AD	AD-LATE STAGE
25	NK	61/F	3	UNDEFINED	AD	AD-LATE STAGE
26	MC	65/M	1	UNDEFINED	FTD	FTD-LATE STAGE
27	VE	62/M	1	UNDEFINED	FTD	FTD-LATE STAGE
28	VG	57/F	2	UNDEFINED	FTD	FTD-LATE STAGE
29	AY	72/F	2	UNDEFINED	FTD	FTD-LATE STAGE
30	ŞK	54/F	3	UNDEFINED	FTD	FTD-LATE STAGE
31	RŞ	55/M	4	UNDEFINED	FTD	FTD-LATE STAGE
32	NK	59/F	1	FTD-EARLY STAGE	AD	AD-LATE STAGE
33	CÇ	68/M	3	FTD-EARLY STAGE	FTD	FTD-EARLY STAGE
34	GG	63/F	3	FTD-EARLY STAGE	FTD	FTD-EARLY STAGE
35	İTG	62/M	3	FTD-EARLY STAGE	FTD	FTD-EARLY STAGE
36	BZ	75/F	2.5	FTD-EARLY STAGE	UNDEFINED	FTD-EARLY STAGE
37	İA	64/M	4	FTD-EARLY STAGE	FTD	FTD-EARLY STAGE
38	PK	54/F	5	FTD-MODERATE STAGE	AD	AD-MODERATE STAGE
39	NE	60/F	2	FTD-MODERATE STAGE	AD	AD-MODERATE STAGE (FRONTAL VARIANT)
40	AE	63/F	2.5	FTD-MODERATE STAGE	AD	AD-EARLY STAGE
41	SP	62/F	1	FTD-MODERATE STAGE	AD	AD-MODERATE STAGE (FRONTAL VARIANT)
42	AG	80/M	3	FTD-MODERATE STAGE	UNDEFINED	FTD-MODERATE STAGE
43	BZG	65/F	2.5	FTD-MODERATE STAGE	UNDEFINED	FTD-MODERATE STAGE
44	GD	65/F	4	FTD-MODERATE STAGE	FTD	FTD-MODERATE STAGE
45	YE	29/F	0.25	FTD-MODERATE STAGE	FTD	FTD-MODERATE STAGE
46	HD	57/F	3	FTD-LATE STAGE	AD	AD-LATE STAGE
47	HFY	70/M	3.5	FTD-LATE STAGE	FTD	FTD-LATE STAGE
48	ŞŞ	63/F	2	FTD-LATE STAGE	FTD	FTD-LATE STAGE

AD: Alzheimer dementia, FTD: frontotemporal dementia.

2.3.2. Assessment of FDG-PET images

Based on the symmetry between the hemispheres, the visual assessment of PET images was performed by evaluating the changes in FDG uptake in both the cortical and subcortical areas. Moreover, the nondiagnostic CT images that were equivalent to the PET sections were reviewed, and the areas with different FDG uptake were examined in order to detect structural abnormalities.

In addition to the visual assessment, the axial sectional images of PET were also evaluated with 3D-SSP software, also known as NEUROSTAT (13). This program was used to compare the counts on each and every image unit (voxel) of the brain images after they were resized and corrected for rotation. The images were imported into a template with the Talairach coordinates in a standard format and were compared with a normal database of matched ages (age ranges of 19–30, 31–54, and 55–91 years). After converting the images to a color scale, the regional deviations (z-score) in the patients were compared to the brain templates, and the standard deviation values were recorded in numerical format from 8 different projections (right lateral, left lateral, superior, inferior, anterior, posterior, right medial, left medial).

2.4. Consensus diagnosis

A probable diagnosis of dementia was agreed upon for each patient (consensus) whose clinical findings and PET images were compatible (Table 4). However, some patients could not be diagnosed due to discordance between the clinical findings and the PET scan or due to the lack of clinical findings (n = 14). A probable diagnosis of dementia was decided for each patient by reevaluating all clinical findings, neuropsychological test results, criteria described in the DSM-IV (NINCDS-ADRDA for AD and/or our own criteria for frontotemporal lobar degeneration), and PET findings together with an expert geropsychologist.

2.5. Statistical assessment

Statistical analyses were conducted using SPSS 16.0 for Windows (SPSS Inc., USA). Numerical data are expressed as mean ± standard deviation, while nominal data are expressed as frequency (n, %) when reporting descriptive statistics. Pearson correlation analysis was used to evaluate linear correlations between the numerical data. The regional z-score distributions in AD and FTD cases were analyzed by histogram graphics. In addition, the differences in the z-scores derived in accordance with the 4 different regional normalizations in each of the 2 disease groups were compared with a McNemar test and Pearson correlation analysis. The differences in the averages of the cortical z-scores between the disease groups were assessed by t-test. $P < 0.05$ was considered statistically significant.

The sensitivity, specificity, accuracy, and negative and positive predictive values of FDG-PET and clinical methods were calculated. In doing so, the consensus diagnosis was considered to be the reference point.

3. Results

According to clinical findings, 17 (35%) patients were diagnosed with probable AD, 17 (35%) with probable FTD, and 14 (30%) with an undefined type of advanced dementia. On the other hand, based on the evaluation of the PET scans, 26 (54%) patients were classified with AD, 19 (40%) with FTD, and 3 (6%) with an undefined type (see Table 3). Dementia type was classified based on the PET scan findings for all of the patients who were unable to be diagnosed by clinical findings (n = 14). However, 3 patients who were not able to be diagnosed by PET images were diagnosed with FTD through consensus diagnosis.

Fourteen of the 34 patients had discordant clinical findings and PET results (9 FTD, 5 AD), while 20 patients (12 AD, 8 FTD) had compatible clinical findings and PET scan results (Table 3). Six of the 9 patients who were clinically diagnosed with FTD were diagnosed with AD by PET scan evaluation and consensus. Three of the 9 patients who were diagnosed with undefined dementia by PET scan were diagnosed with FTD through consensus. Two of the 5 patients who were clinically diagnosed with AD were determined to have FTD by PET scan evaluation, while 3 of them were diagnosed with FTD through consensus (Table 4).

Fourteen patients with clinically undefined advanced dementia had agreement between their PET scan and consensus diagnosis. Accordingly, 8 of the 14 patients

Table 3. Consistency table for the clinical and PET diagnoses.

	Clinical diagnosis			
PET diagnosis	Alzheimer dementia	Frontotemporal dementia	Undefined dementia	Sum
Alzheimer dementia	12	6	8	26
Frontotemporal dementia	5	8	6	19
Undefined dementia	0	3	0	3
Sum	17	17	14	48

Table 4. Consistency of consensus diagnosis with clinical and PET diagnoses.

	Consensus diagnosis		
PET diagnosis	Alzheimer dementia	Frontotemporal dementia	Sum
Alzheimer dementia	26 (54%)	0	26
Frontotemporal dementia	2 (4%)	17 (35%)	19
Undefined	0	3 (6%)	3
Clinical diagnosis			
Alzheimer's dementia	14 (29%)	3 (6%)	17
Frontotemporal dementia	6 (12.5%)	11 (23%)	17
Undefined	8 (17%)	6 (12.5%)	14

were diagnosed with AD (Figures 1A and 1B), and 6 of the patients were diagnosed with FTD (Figures 2A and 2B; Table 4). Consensus diagnosis was compatible with PET scan results in 43 (90%) of the 48 patients, while the clinical findings were compatible with consensus diagnosis in only 25 (52%) patients (Table 4). In 23 of the 28 (82%) patients with inconsistent results between the PET scan and clinical findings, consensus results were compatible with results from the PET scan, and in 5 of 28 (18%) patients, consensus was compatible with clinical features. When the 5 patients for whom the consensus diagnosis was in favor of PET were examined, 2 were considered to have AD through clinical diagnosis and FTD according to PET findings, and they were diagnosed with frontal variant AD through consensus diagnosis. Three patients with clinically diagnosed FTD and atypical PET findings were diagnosed with FTD through consensus.

Since there was good consistency ($r > 0.85$) and no significant differences between z- score values derived from the normalizations of different reference cortical regions (total cerebrum, thalamus, cerebellum, and pons) by NEUROSTAT analysis, total cerebrum normalization was considered as a reference point for all related analyses and assessments (Table 5).

The z-score values derived from parietal, temporal, frontal, occipital, posterior cingulate, and anterior cingulate areas (normalized with total cerebrum) were categorized by type and the stage of dementia (Table 6). Average z-scores are defined as the loss of metabolic activity in the posterior cortical regions (parietal, occipital, and posterior cingulate). The average z-scores of the AD patients were significantly higher than those of the FTD patients (Figure 3). Conversely, no significant difference was found between the AD and FTD groups with regards

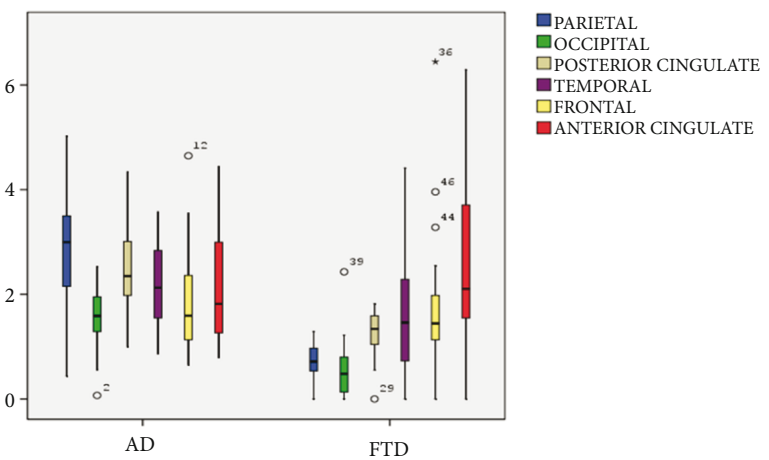

Figure 1. The distribution of z-scores in the specific cortical regions in the AD and FTD groups. Numbers near circles represent the number of the patient in Table 2.

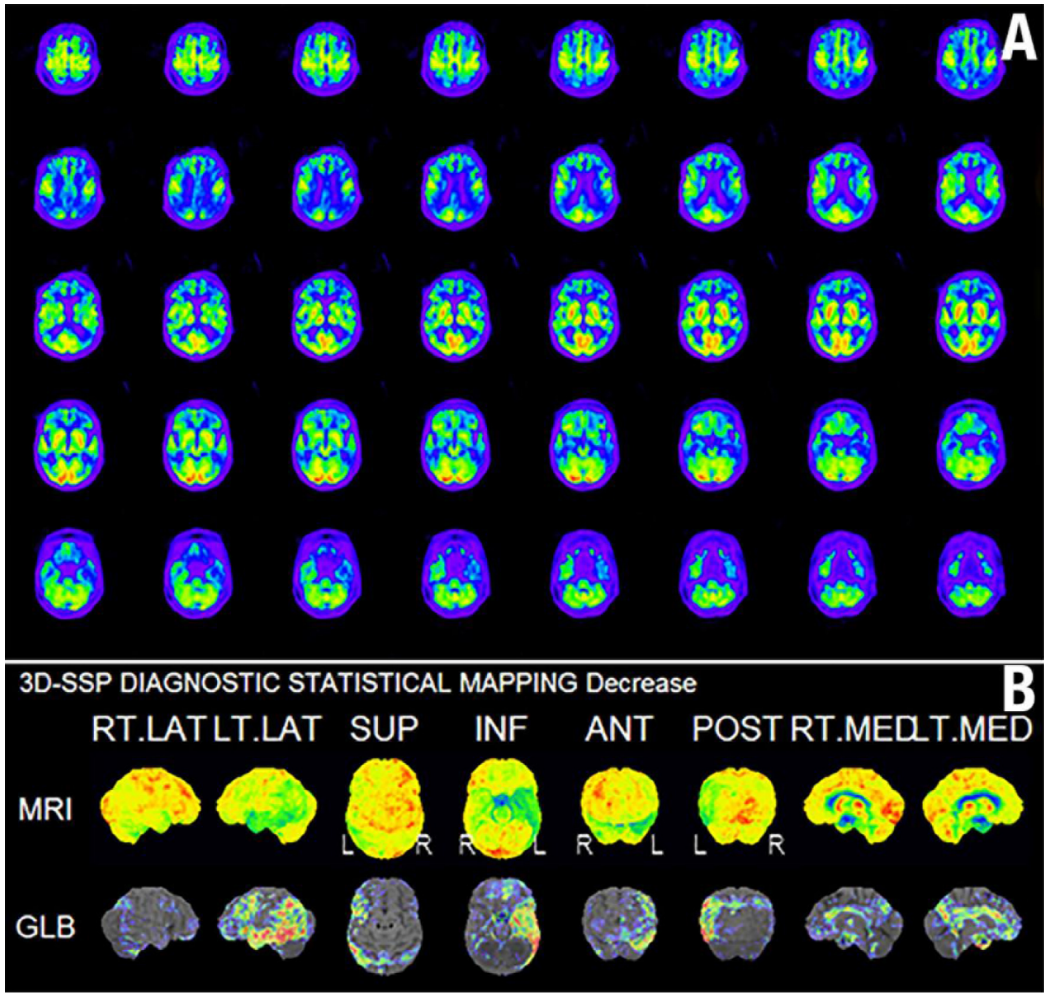

Figure 2. Case no. 24: **(A)** Assessment of the neuropsychometric tests and clinical findings revealed a significant decrease in FDG uptake in all anterior and posterior cortical regions [other than the primary motor and sensorial regions and visual cortexes (occipital cortical regions)] in the axial FDG-PET brain images of a 68-year-old female patient with an early diagnosis of undefined advanced dementia. **(B)** Obvious z-score deviations in accordance with the 55–91 year age range average were observed in 3D-SSP (NEUROSTAT) images in the bilateral temporo-parietal-occipital, bilateral posterior, anterior cingulate, and bilateral frontal regions. This image resembles advanced-stage Alzheimer disease. The patient was diagnosed with Alzheimer disease through consensus diagnosis.

Table 5. The consistency of the z-scores derived from different normalizations.

AD	Total cerebrum normalization & thalamus normalization	r = 0.858
	Total cerebrum normalization & cerebellum normalization	r = 0.842
	Total cerebrum normalization & pons normalization	r = 0.814
FTD	Total cerebrum normalization & thalamus normalization	r = 0.978
	Total cerebrum normalization & cerebellum normalization	r = 0.930
	Total cerebrum normalization & pons normalization	r = 0.941

to the scores of the frontal, anterior cingulate, and temporal regions.

Cortical z-scores are evaluated throughout the stages of dementia. In the early-stage AD group (although the patient number was low), pathological change ($Z > 1.5$) was only observed in the posterior cingulate cortex. The patients with moderate and advanced AD also had pathological changes in z-scores for the parietal, temporal,

Table 6. The distribution of the regional cortical z-score averages according to the disease groups and stages.

Classification of consensus diagnosis	Parietal		Temporal		Frontal		Occipital		Posterior cingulate		Anterior cingulate	
	R	L	R	L	R	L	R	L	R	L	R	L
Early-stage AD (n = 3) (mean ± SD)	0.99 ± 0.69	0.9 ± 0.36	1.48 ± 09	0.89 ± 0.16	1.32 ± 0.76	1.06 ± 0.38	0.45 ± 0.27	0.42 ± 0.38	1.76 ± 0.31	1.65 ± 0.51	2.07 ± 1.43	2.13 ± 1.47
Moderate-stage AD (n = 12) (mean ± SD)	3.26 ± 1.28	2.88 ± 1.08	2.13 ± 1.18	2.02 ± 0.8	2.03 ± 1.15	1.58 ± 1.14	1.55 ± 0.68	1.71 ± 0.49	3 ± 0.87	2.64 ± 0.69	1.96 ± 1.07	1.92 ± 0.92
Late-stage AD (n = 13) (mean ± SD)	2.7 ± 0.97	3.2 ± 0.89	2.22 ± 0.98	2.66 ± 0.9	1.83 ± 0.9	2.16 ± 0.9	1.53 ± 0.73	1.92 ± 0.73	2.36 ± 0.88	2.49 ± 0.94	2.17 ± 1.15	2.44 ± 0.95
Sum of the AD group (n = 28) (mean ± SD)	2.63 ± 1.29	2.67 ± 1.18	2.04 ± 1.09	2.09 ± 0.99	1.81 ± 1.03	1.72 ± 1.06	1.35 ± 0.76	1.59 ± 0.76	2.47 ± 0.94	2.37 ± 0.86	2.05 ± 1.14	2.16 ± 1.02
Early-stage FTD (n = 7) (mean ± SD)	0.78 ± 0.3	0.57 ± 0.17	1.22 ± 0.91	1.3 ± 0.8	2.03 ± 1.99	2.02 ± 1.97	0.59 ± 0.45	0.58 ± 0.47	1.46 ± 0.17	1.49 ± 0.23	2.28 ± 1.56	2.42 ± 1.49
Moderate-stage FTD (n = 6) (mean ± SD)	0.62 ± 0.4	0.96 ± 0.44	1.99 ± 1.33	2.37 ± 1.16	1.29 ± 0.39	1.87 ± 1.01	0.45 ± 0.68	0.82 ± 1.02	1.12 ± 0.47	1.24 ± 0.48	2.55 ± 1.89	2.93 ± 1.81
Late-stage FTD (n = 7) (mean ± SD)	0.84 ± 0.42	0.72 ± 0.35	1.82 ± 1.62	1.96 ± 1.05	1.98 ± 1.17	2.16 ± 1.18	0.52 ± 0.47	0.55 ± 0.57	1.17 ± 0.33	1.3 ± 0.33	3.05 ± 1.61	3.22 ± 1.39
Sum of the FTD group (n = 20) (mean ± STD)	0.75 ± 0.38	0.74 ± 0.36	1.66 ± 1.33	1.85 ± 1.09	1.79 ± 1.36	2.02 ± 1.42	0.52 ± 0.53	0.64 ± 0.72	1.26 ± 0.37	1.35 ± 0.37	2.63 ± 1.68	2.85 ± 1.57
AD & FTD (t-test P-value)	<0.0001	<0.0001	0.166	0.224	0.872	0.333	<0.0001	<0.0001	<0.0001	<0.0001	0.133	0.058

AD = Alzheimer dementia, FTD = frontotemporal dementia, R = right, L = left.

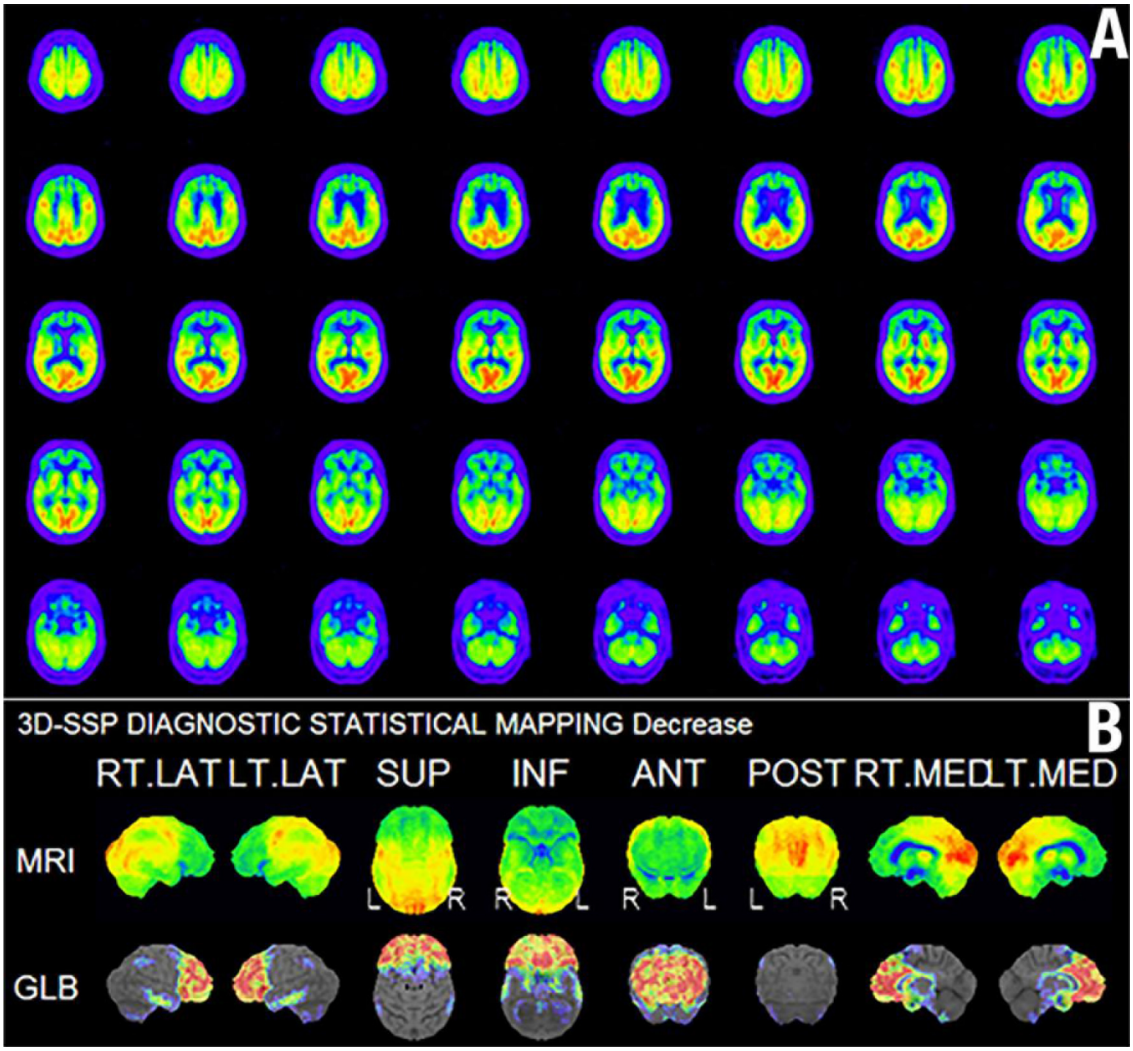

Figure 3. Case no. 30: **(A)** Assessment of the neuropsychometric tests and clinical findings revealed that there was a significant decrease in FDG uptake in the bilateral frontal lobes, which also partially expanded to the temporal regions in the axial FDG-PET brain images of a 54-year-old female patient whose type of dementia could not be defined and was therefore diagnosed with undefined advanced dementia. This resembles frontotemporal dementia. Hypometabolism was observed in the same regions in accordance with the **(B)** 31–55 year age range average in the 3D-SSP (NEUROSTAT) images. This was defined as frontotemporal dementia through consensus diagnosis.

occipital, frontal, and anterior cingulate regions, as well. In early-stage FTD patients, the z-scores of the temporal region were relatively normal. In addition, the z-scores of the frontal and anterior cingulate regions were affected similarly in all stages of FTD.

When consensus diagnosis is considered as the reference, the sensitivity, specificity, accuracy, and positive and negative predictive values of PET scan for the diagnosis of AD were 93%, 85%, 90%, 90%, and 89%, respectively. On the other hand, the sensitivity, specificity, accuracy, and positive and negative predictive values of PET scan for the diagnosis of FTD were 85%, 93%, 90%, 89%, and 90%, respectively.

4. Discussion

In AD, neurodegeneration develops in the temporo-parietal-occipital cortex and in the frontal lobes stemming from the posterior cingulate cortex. FDG-PET scanning shows a typical hypometabolic distribution pattern in these affected regions. Several studies have reported that PET scan is a useful method in both the diagnosis of AD and in the differentiation of different types of dementia. Silverman et al. reported that 91 of 97 AD patients were accurately diagnosed with a PET scan (sensitivity: 94%), and this diagnosis was verified with postmortem neuropathological examinations. On the other hand, in those with non-AD dementia, the absence of AD was

accurately depicted by PET in 30 of 41 patients (specificity: 73%). Additionally, that published study indicated that the development of a cognitive deformity was very low (negative probability rate: 0.10; 95% CI: 0.06–0.16) based on a follow-up of on average 3 years in patients with normal PET scans (10). Patwardhan et al. conducted a metaanalysis of 15 studies that were published between 1989 and 2003 regarding the contribution of FDG-PET in the diagnosis of AD. The heterogeneous distribution of the sensitivity and specificity values was 86% (95% CI: 76%–93%) and 86% (95% CI: 72%–93%), respectively. The heterogeneous distribution could not be explained, which indicates that the sensitivity and specificity of FDG-PET may be limited. A recently published summary of 5 studies, in which a new-generation PET scanner was used, indicated that the accuracy, sensitivity, and specificity of FDG-PET in the diagnosis of AD were 93%, 96%, and 90%, respectively (4).

In our study, the consensus diagnosis was considered as the reference point, and the sensitivity, specificity, accuracy, and positive and negative predictive values of PET in the diagnosis of AD were 93%, 85%, 90%, 90%, and 89%, respectively. In addition, the sensitivity, specificity, accuracy, and positive and negative predictive values of PET in diagnosing FTD were 85%, 93%, 90%, 89%, and 90%, respectively. Since our results were obtained from selected patient groups and were not based on a definitive reference for diagnosis, there may be doubts regarding the reliability of this study. However, that FDG-PET was able to determine the type of dementia for 14 (29%) clinically undiagnosed cases in agreement with the consensus diagnosis indicates the usefulness of this method.

Jagust et al. reported that FDG-PET (sensitivity: 84%, specificity: 74%) is better for diagnosing AD than a clinical assessment in the early stages (sensitivity: 76%, specificity: 58%) (14). Similarly, Foster et al. stated that FDG-PET (sensitivity: 96.7%, specificity: 85.7%) is superior to clinical methods in the differential diagnosis of FTD and AD (15).

In the current study, the mean z-score values of AD patients were significantly higher than those of the FTD group in the posterior cortical regions (parietal, occipital, and posterior cingulate). On the other hand, the mean z-score values in the anterior cortical regions (frontal, anterior cingulate, and anterior temporal) were higher in patients with FTD, but no significant difference was found between the AD and FTD patient groups. This is an unexpected observation that may be explained by the fact that the anterior cortex is affected in addition to the posterior cortex regions, since most of the AD patients in our study were considered to be in the middle/advanced stages of the disease. Therefore, we observed a considerable similarity of metabolic distribution patterns between the AD and FTD patients in these regions, with the exclusion of the parietal and occipital cortexes.

The assessment of ^{18}F-FDG PET images requires experience; the evaluator must be familiar with the normal changes that are associated with aging in cerebral glucose metabolism. It is very difficult to distinguish the posterior cingulate gyrus activity by visual assessment, especially when diagnosing early-stage AD. Furthermore, even experienced physicians can have discordant results with visual assessments (16). Statistical parametric mapping software (SPM, NEUROSTAT, etc.) that is capable of assessing the cerebral cortical counts with a normal database on a voxel basis and performing quantitative analysis has been developed in order to reduce these inconsistencies (17). The variations between physicians can be significantly decreased by using this software, which is more objective in assessment (13). This software can be efficiently used for assessing deep and small cortical regions, such as the posterior cingulate gyrus, which is difficult to evaluate by visual assessment (18).

Minoshima et al. explained how the 3D-SSP program can be used for evaluating FDG-PET brain images for diagnosing AD (13). This program was also used in our study for analyzing the images, in addition to visual assessment. To our knowledge, we are the first to use this program in Turkey. Since the program's database is originally from North America, a national database integrated to the program is required for Turkey. However, it should be kept in mind that this type of software can be affected by patient movement, by faulty positioning of the patient during imaging, or by an already existing structural deformity within the brain. Ultimately, these types of automatic analysis programs should be used, but only when backed up by visual assessment and clinical information.

In conclusion, FDG-PET imaging can be a beneficial method for the evaluation of dementia diseases, especially in cases where the clinical findings are nondifferentiating, the type of dementia cannot be defined with neuropsychological tests, or the physician is not certain about the diagnosis. This study had a limited number of patients, but we found that the diagnostic accuracy of FDG-PET scanning was significant for the clinical diagnosis of both AD and FTD. Furthermore, using 3D software in addition to the visual assessment of brain FDG-PET images can increase the diagnostic accuracy and decrease the variability in the interpretations by different physicians/centers.

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