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Research Article

Are Brain SPECT Data and Neuropsychological Disturbances Correlated in Patients With Alzheimer Disease and Vascular Dementia?

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Summary

Background: The clinical identification and the role of imaging in the differential diagnosis of dementia is challenging. The aim of this study is to investigate the characteristics and correlation of neurophsychological test battery and the semi-quantitative brain SPECT imaging in Alzheimer's Dementia(AD) and Vascular Dementia (VaD).
Methods: A total of 56 AD and 16 VaD patients, and 16 patients in the control group were evaluated by neurophsychological test battery and 99mTc-HMPAO brain SPECT study. All of the patients underwent detailed neurological examination, cerebral magnetic resonance imaging, and laboratory evaluation before diagnosis. Regional perfusion ratios were calculated in brain SPECT study and compared with neurophsychological test results.
Results: Demographic characteristics (age, gender, education) were identical in AD, VaD and control group. In brain SPECT study regional perfusion ratio of posterior cingulate was significantly lower in AD group than control subjects (p=0.030). Mini Mental State Examination was identical in AD and VaD patients, but there was statistically significant difference between study groups when compared with control subjects (p=0.001). There were significant correlations between neuropsychiatric test results and regional perfusion ratios.
Conclusions: The results of this study confirms that regional perfusion defects correlate with specific patterns of cognitive abnormalities in AD and VaD. Brain SPECT imaging accompanied by detailed neurophsychological battery helps us to understand the degree of cerebral functioning more accurately and would increase gain in diagnostic certanity in clinical practice.

Key words: Alzheimer's disease, Vascular Dementia, SPECT, semi-quantitative analysis, neurophsychological battery

Alzheimer ve Vasküler Demans Hastalarinda Beyin Spect Datasi ve Nöropsikolojik Bozukluklar İlişkili midir?

Özet

Amaç: Demansın ayırıcı tanısında klinik tanımlama ve görüntülemenin rolü zorludur. Bu çalışmanın amacı vasküler demans (VaD) ve Alzheimer Hastalığında (AH) nöropsikolojik test bataryası ve beyin SPECT görüntülemenin ilişkisini araştırmaktır.
Yöntem: 56 AH ve 16 VaD hastası ve 16 kişilik kontrol grubu, nöropsikolojik test bataryası ve Tc-99m HMPAO beyin SPECT çalışması ile değerlendirildi. Bütün hastalara tanı öncesinde ayrıntılı nörolojik muayene ve laboratuvar tetkikleri ve beyin manyetik rezonans

görüntülemesi yapıldı. Beyin SPECT çalışmasında semikantitatif olarak hesaplanan bölgesel perfüzyon oranları, nöropsikolojik test sonuçları ile karşılaştırıldı.
Bulgular: Demografik özellikler (yaş, cinsiyet, eğitim) açısından AH, VaD ve kontrol grubunda farklılık saptanmadı. Beyin SPECT çalışmasında posterior singulatın bölgesel perfüzyon oranı, AH grubunda kontrol grubuna kıyasla belirgin olarak düşüktü (p = 0.030). Mini Mental Durum Testi, AH ve VaD hastalarında benzer bulundu ancak, kontrol grubu ile karşılaştırıldığında çalışma grupları arasında istatistiksel olarak anlamlı farklılık mevcuttu(p = 0.001). Nöropsikiyatrik test sonuçları ve bölgesel perfüzyon oranları arasında anlamlı ilişki saptandı.
Sonuç: Bu çalışmanın sonuçları, AH ve VaD hastalarında bölgesel perfüzyon defektlerinin spesifik bilişsel anormallikler ile ilişkili olduğunu desteklemektedir. Ayrıntılı nöropsikolojik batarya eşliğinde Beyin SPECT datası serebral işleyişi ve düzeyini daha doğru anlamamıza, klinik pratikte de tanı keskinliğinin artırılmasına yardımcı olacaktır.

Anahtar Kelimeler: Alzheimer Hastalığı, Vasküler Demans, SPECT, semi-kantitatif analiz, nöropsikolojik testler

INTRODUCTION

Neurorodegenerative diseases are very common; however clinical symptoms and signs are subtle until neurodegeneration is advanced. This is evident for Alzheimer's disease (AD), vascular dementia (VaD), Parkinson's disease and for many other neurodegenerative diseases. The need for early and accurate diagnosis has become more important since several medications for the treatment of mild to moderate AD has been introduced. Similarly, patients with vascular risk factors or early signs of VaD could benefit from effective treatment with antihypertensive, antitrombotic or surgical regimens.

Classically neuroimaging is indicated for ruling out mechanical causes of demential syndromes (tumors, subdural hematoma, etc). But today considerably improved functional neuroimaging techniques, such as functional MRI, single-photon emission computed tomography (SPECT) and positron emission tomography (PET) can provide us more knowledge about the brain functions, and can help us to understand[1,6,23,24].

Functional impairment in cerebral diseases often precedes structural changes. SPECT is a sensitive method for detecting impairment of regional cerebral function even when CT or MRI reveal no spesific findings. Different perfusion patterns have been associated with different types of dementia[4]. The location of dementia associated metabolic impairment and age related decline in normals are seperate from each other. The findings of cerebral hypoperfusion in the bilateral posterior cingulate gyri, precunei, and inferior parietal cortex of the brain using PET and SPECT, and the quantitative analysis of images have been established as early diagnostic tools of AD[3,10,13,16]. A limiting factor is that, all these techniques may not be available for every center. Another question is the increased cost of the diagnostic process and economical burden of the disease. Which is the best diagnostic method for dementia disorders? Actually, the answer is not definite. The contribution of a sensitive, relatively cheap and a practical battery which can be completed in a short span of time cannot be opposed.

In this study we aimed to define the correlation of the semiquantitative ^{99m}Tc-HMPAO brain SPECT results and the neurophsychological test battery and investigate associations between regional brain perfusion defects and clinical

variables for the diagnosis of the mostly seen demential syndromes AD and VaD.

MATERIAL AND METHODS

Patients

A total of 88 subjects were included in this study. Fifty-six demented patients with AD, and 16 with VaD were studied and compared with those of 16 age-matched controls. The entire subject's recruited from the Dementia Outpatient Department of Neurology Clinics and controls composed from the voluntary healthy spouses of the patients. All of the subjects and their legal representatives gave written informed consent to the study protocol which was approved by Local ethical committee. All of the subjects underwent detailed neurological examination by the same neurologist. Both of the study and the control group underwent ophthalmologic and audiologic examinations to exclude visual or hearing deficits, which might compromise the reliability and validity of the neuropsychological testing. The demographical properties of the patients were identical enough to enable clinical comparison.

Patients with any visual or auditory deficit, and neuropsychological disturbances (delirium, severe psychosis, etc) restricting SPECT application were not included in the study. Healthy controls were composed from the voluntary spouses of the patients after detailed neurological and short neuropsychological evaluation including Mini Mental State Examination (MMSE).

Dementia diagnosis

All AD cases met the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria of probable AD[19]. All subjects underwent a detailed biochemical screening (including thyroid function testing, B_{12}-Folic acid level, malignancy screening, etc) and radiological investigation (Cranial CT or MRI) before dementia diagnosis. If needed, additional investigations have also been made (i.e. EEG). All VaD patients met the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neuroscience (NINDS-AIREN)[22].

Neuropsychological test batteries

Neuropsychological evaluation included following tests;

Standardized Mini Mental State Examination (SMMSE)

MMSE is a brief, simple, widely used cognitive tool and evaluate cognition in several domains. It is a 30 points scale, resulting from following subscales; orientation to time, orientation to place, registration, attention/calculation, recall, language naming, repeat phrase, 3 step command, comprehension, sentence construction, copy figure. We have used a version of MMSE (SMMSE) by Güngen et al., taking into consideration of formal education level who found that the cutoff score 23/24 have highest sensitivity (0.91), specificity (0.95), positive and negative predictive values and kappa score 0.90, 0.95, and 0.86 respectively[8].

Daily Living Activity Scale

Daily living activity scale measures patient's independence and capabilities of daily living activities. Since daily activities decline in early stages of dementia, this scale is widely used for detecting dementia. It is scored if the patient needs little or no help in complex tasks such as household finances, shopping or cooking. Total score range is 0 to 23.

Daily Habituations Scale

Daily habituations scale is used to measure patients' capability for daily habituations. It is a caregiver based scale and asked to caregiver to rate about the patient's eating, dressing oneself and sphincter control habituations. Total score range is 0 to 9.

Clock DrawingTest

Clock drawing is a simple task and generally used to screen dementia. Drawing a clock necessitates multiple cognitive abilities such as visuo-spatial organization, constructional abilities and executive functions. In this research pre-drawn method and 10 point scale were used[17].

Digit Span

Digit span recall has been widely used in neurological research and clinical evaluation to assess attention abilities, short- term memory and working memory. Digit forward requires participants to repeat digits which are represented orally and sequentially in increasing length. Digit backward requires to repeat digits in reversed order. In this battery total score range is 0 to 14.[2,12].

Counting

In present study, counting task was used to assess calculating abilities. Arithmetic skills are important in everyday habituations and related with various daily living activities such as shopping, household finances, managing financial budget. In this battery total score range is 0 to 5.[29]

Abstract thinking

Since proverbs are generally brief, abstract has deeper meaning than concrete meaning, it requires executive functions such as fundamental language skills and abstract thinking[18]. In present study we asked patients 3 proverbs to assess their abstracting abilities. Total score range is 0 to 3.

Praxis

Participants were asked to perform 5 spoken commands, included toll-use gestures such as “Show me how you would open the door with a key” and tool-free gestures such as waving good bye. Both hands movement is known to activate the inferior parietal lobule, supplementary motor area and premotor area of left hemisphere[30]. In this battery total score range is 0 to 13.

Boston Naming Test

In this study, shortened version of Boston Naming Test was used to evaluate participants' visual naming performance and lexico-semantic abilities. Fifteen drawing line objects were shown to participants and asked to name each object, not usage of it. Adequate evidence showed that naming task can be shown to involve left inferior prefrontal and posterior temporal cortex[15,21]. Also Obler et al., suggested that right hemisphere regions related to left hemisphere languages areas, involved in lexical-retrieval in older adults[20]. In this battery total score range is 0 to 15.

Construction Test

Four line drawing figures of CERAD Drawing test, (a circle, a diamond, intersecting rectangles, a cube) in increasing complexity were used. Participants were asked to copy these figures. Essentially copying figure requires multifunctional cognitive abilities. Förster et al. showed that visuo-constructive test correlated with bilateral inferior temporal gyri, bilateral precuneus, right cuneus, right supramarginal gyrus and right middle temporal gyrus covering areas of dorsal and ventral visual streams[7]. In this battery total score range is 0 to 11.

Neuro-psychiatric Inventory (NPI) total

NPI is designed to detect or tract the behavioral and psychiatric symptoms in demented patients. It uses as a caregiver based inventory to assess problematic behaviors in 12 domains (delusions, hallucinations, agitation, dysphoria, anxiety, apathy, euphoria, disinhibition, aberrant motor behavior, nighttime behavioral disturbance and appetite/weight change). At first the existence of symptoms are asked to caregiver particularly in a yes/no format. If the answer is yes, caregiver is asked to rate the frequency of occurrence of problematic behavior. Then

behaviors are rated on level of severity. The domain total score is the product of the frequency score multiplied by the severity score for each domain[5]. In this battery total score range is 0 to 120.

Clinical Dementia Rating (CDR) Scale

CDR was developed to use for staging the dementia. It is a five point scale of each subdomain (composed from 6 subdomains) reaching a CDR score from "0" to "3" with increasing cognitive impairment. In assigning impairment six domains (memory, orientation, judgment and problem-solving, community affairs, home and hobbies and personal care) are used. These domains are rated considering patient's cognitive ability to function in these areas.

Global Deterioration Scale (GDS)

GDS was proposed in and allows professionals and caregivers to chart the decline of people with dementia. While a number of scales exist, GDS is one of the most widely used instrument to stage the course of AD. It measures cognitive, behavioral and functional impairment of patients. There are a total of 7 GDS stages (from stage 1 corresponding to no impairment to stage 7 corresponding to the most severe impairment)[14].

SPECT imaging protocol

All subjects were examined in an identical setting. Any medication known to affect overall brain perfusion (e.g. vasodilators) was discontinued at least 48 hours before SPECT scan. Regional cerebral blood flow (rCBF) has been evaluated using a double headed Gama camera (Siemens, E-CAM, USA) equipped with high resolution, parallel hole collimators. Seven hundred and forty MBq of ^{99m}Tc hexamethyl proplene amine oxime (^{99m}Tc-HMPAO) were injected intravenously while the patient was sitting, in a room with dim lighting, ears unplugged. Patients were instructed not to speak, read, or move from at least 5 min before to 5 min after injection. Before acquisition, only 1 patient was administered sedative medication 20 min after tracer injection.

Sixty minutes after the radiopharmaceutical administration, SPECT imaging was performed. During a 360 degrees NCO rotation, 128X30sec frames in 128X128 matrix images were obtained. The raw data were reconstructed parallel to the orbito-meatal line using filtered back projection with a Butterworth filter (cut off: 0.28, order: 10) and attenuation correction was carried out using Chang's method (μ: 0.12).

Visual interpretation of the brain perfusion scintigraphy was assesed in consensus by 2 nuclear medicine specialists with 10 years of experience on brain SPECT who had no knowledge of the clinical data. The distribution of radioactivity in the cerebral and cerebellar regions, focal or global perfusion differences, asymmetry, unilateral or bilateral decreased areas of perfusion were evaluated.

Regions of interest (ROI) were manually drawn over the frontal, parietal, temporal, and occipital lobes, and cerebellum on consecutive transaxial slices according to Talairach coordinates[26], and mean counts (total counts/pixel size) were calculated for each ROI throughout the brain. Limbic region, anterior and posterior cingulate gyrus were also evaluated semiquantitatively. Regional ratios to cerebellum (regional perfusion ratios) were calculated using mean counts.

Statistical analysis

Distributions of the data were analyzed with Shapiro-Wilks test, and parametric or non-parametric methods were used according to the test result. Independent samples t test or Mann-Whitney U test for comparing two groups and One-Way ANOVA or Kruskal-Wallis test for comparing three or more groups were used. Pearson Correlation or Spearman Rank Correlation used for analyzing linear association between continuous data, and chi-square test was used for categorical

data. Statistical analyses were done by SPSS v.11.5 package and p values equal or less than 0.05 were regarded as statistically significant. Mean and standard deviation for continuous data, and frequency and percent for categorical data were presented.

RESULTS

Patients with AD, VaD and control group were not statistically different from each other with regard to age, sex or formal education time (Table 1). Duration of disease and family history for dementia were also identical in AD and VaD group (p>0.05).

Neuropsychological screening results were as follows;

SMMSE was identical in AD and VaD patients, but there was statistically significant difference between study groups when compared with control subjects (p=0.001). In AD and VaD patients CDR, GDS, daily living activity and habituations scale, clock drawing, forward and backward digit span, abstraction, praxis, understanding, Boston naming and construction test, NPI-total were not statistically different from each other (p>0.05) (Table 2).

Visual evaluation of SPECT images revealed that the altered brain perfusion areas were mostly seen in bilateral parietal and temporal regions in AD group (61.4 %) (Figure 1a). However, frontal lobe deficits in conjunction with temporoparietal abnormalities were also detected in 16 (28.6%) patients. Regional perfusion ratio of posterior cingulate was significantly lower in AD group than control subjects (p=0.030). When compared to control group; bilateral parietal, temporal and frontal lobe deficits were also confirmed by using regional perfusion ratio calculations (p<0.05) (Table 3).

In VaD group, 12 of 16 patients (75%) showed asymmetric perfusion abnormalities (Figure 1b). In 4 (25%) patients, patchy CBF abnormalities accompanied with bilateral parietal or temporal hypoperfusion were detected. In despite of visual evaluation, the difference between mean regional perfusion scores of VaD and control group did not reach to a statistically significant level.

In AD group, perfusion defects in limbic region (r=-0.414, p=0.008) and anterior cingulate gyrus (r=-0.352, p=0.026) were statistically correlated to duration of the disease. (Figure 2a). There were also significant correlations between regional perfusion ratios and neuropsychiatric evaluation scores as follows;

• limbic region and recording subscore of SMMSE (r=-0.274,p=0.045)

• right frontal region and CDR (r=-0.278, p=0.038)

• left temporal region and backward counting (r=0.298, p=0.042),

• right parietal region and recording (r:-0.365, p:0.007) and time-place orientation (time r:-0.312 p:0.022, place: r:-0.270 p:0.048)

In VaD group, perfusion defects in posterior cingulate (PS) and limbic region (L) were correlated with SMMSE (L1: r =0.761, p=0.001, PS: r =0.586, p=0.017), GDS (L1: r = -0.646, p=0.007; L2: r =-0.550, p=0.027; PS: r =-0.531, p=0.034) and CDR (L1: r =-0.537 p=0.032; L2: r =-0.579, p=0.019, PS: r =-0.614, p=0.011) (Figure 2b). There were also significant correlations between perfusion defect regions and clinical parameters as follows;

• right frontal region with CDR (r =-0.507 p=0.045), habituations (r =-0.592, p=0.026), daily living activity scores (r =-0.581, p=0.037)

• right parietal region with CDR (r =-0.547 p=0.028) and orientation to time (r =-0.518 p=0.048)

• right temporal region with orientation to time (r =-0.746, p=0.001), place (r =-0.615

p=0.015) and recording (r =-0.636, p=0.011)

• left parietal (LP) and left temporal(LT) regions with short term memory (LP: r =+0.647, p=0.007; LT: r =+0.734, p:0.001) and language subscores of SMMSE (LP: r=+0.647, p=0.007; LT: r=+0.527, p=0.036)

• left frontal region with short term memory subscores of SMMSE (r=+0.606, p:0.013)

Table 1. Demographic features of the study subjects

	AD (n=56)	VaD (n=16)	Controls (n=16)
Age (mean±SD)	74 ± 9	77 ± 8	67± 12
Gender (male/female) n (%)	21/35 (37.5/62.5)	11/5 (68.7/31.3)	7/9 (44.3/55.7)
Formal education (year) (mean±SD)	7.3 ± 3.9	7.25 ± 4.3	7.5 ± 3.5
Duration of disease (year) (mean±SD)	3.8 ± 2.6	2.6 ± 1.5	-
Positive family history for dementia n (%)	13 (34.2%)	2 (13.3%)	-

[#] There is no significant difference between the groups according to the demographic features

Table 2. Neuropsychological screening results of the patients.

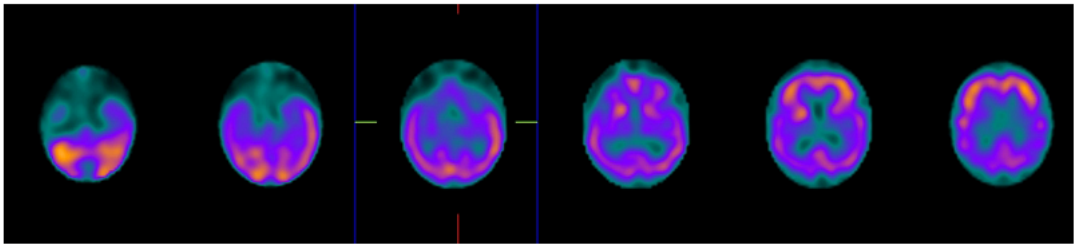
	AD (n=56)	VaD (n=16)
*SMMSE (mean±SD)	18.05 ± 6.34	17.94 ± 7.25
Daily Living Activity Scale	8.00 [3.25-14.00]	5.00 [1.5-11.50]
Daily Habituations Scale	1.00 [0.00-3.00]	2.00 [1.00-2.25]
*Clock Drawing test	4.38 ± 3.53	3.63 ± 3.24
Digit span- Forward	4.00 [3.00-4.00]	4.00 [2.75-4.25]
Backward	2.00 [0.0-2.00]	2.00 [0.00-2.00]
Counting	1.00 [0.00-3.00]	2.00 [0.00-3.00]
Abstraction	2.00 [1.00-3.00]	1.00 [1.00-2.00]
Praxis	13.00 [10.25-13.00]	13.00 [11.75-13.00]
Understanding	6.00 [6.00-6.00]	6.00 [5.00-6.00]
Boston Naming Test	7.00 [5.75-10.00]	6.00 [4.50-8.50]
Construction Test	4.00 [2.00-7.00]	4.00 [1.50-10.00]
NPI-total	14.00 [9.50-22.00]	18.50 [11.75-36.50]
CDR	1.00 [1.00-1.00]	1.00 [0.63-1.75]
GDS	4.00 [3.00-4.00]	4.00 [3.00-4.00]

*Figures represents as (mean±SD), others median [25- 75]

Table 3. Regional perfusion ratios of the patients and the control group

	AD (n=56)	VaD (n=16)	Control (n=16)
Right Temporal	0.75 ± 0.06	0.78 ± 0.11	0.79 ±0.08
Left Temporal	0.68 ± 0.08	0.71 ± 0.08	0.82 ± 0.11
Right Frontal	0.76 ± 0.07	0.77 ± 0.13	0.88 ± 0.07
Left Frontal	0.76 ± 0.07	0.77 ± 0.09	0.87 ± 0.07
Limbic	0.83 ± 0.11	0.83 ± 0.24	0.86 ± 0.14
Anterior cingulate	0.85 ± 0.11	0.87 ± 0.21	0.86 ± 0.13
Posterior cingulate	0.78 ± 0.10	0.85 ± 0.18	0.87 ± 0.14
Right parietal	0.79 ± 0.07	0.91 ±0.11	0.88 ± 0.04
Left parietal	0.79 ± 0.06	0.92 ± 0.08	0.88 ± 0.05

Values represented as mean±SD.



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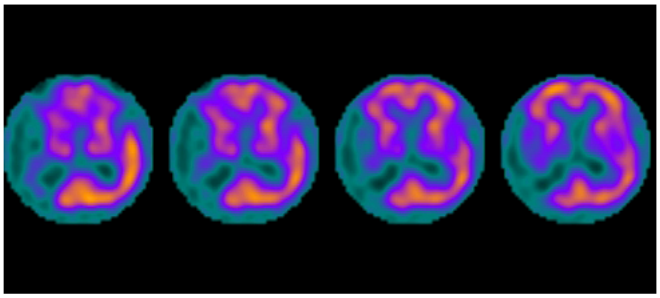

B

Figure 1a-b: *Brain perfusion images showing decreased perfusion in temporal and parietal lobes in AD (a) and left occipitotemporal region in a VaD (b) patient.*

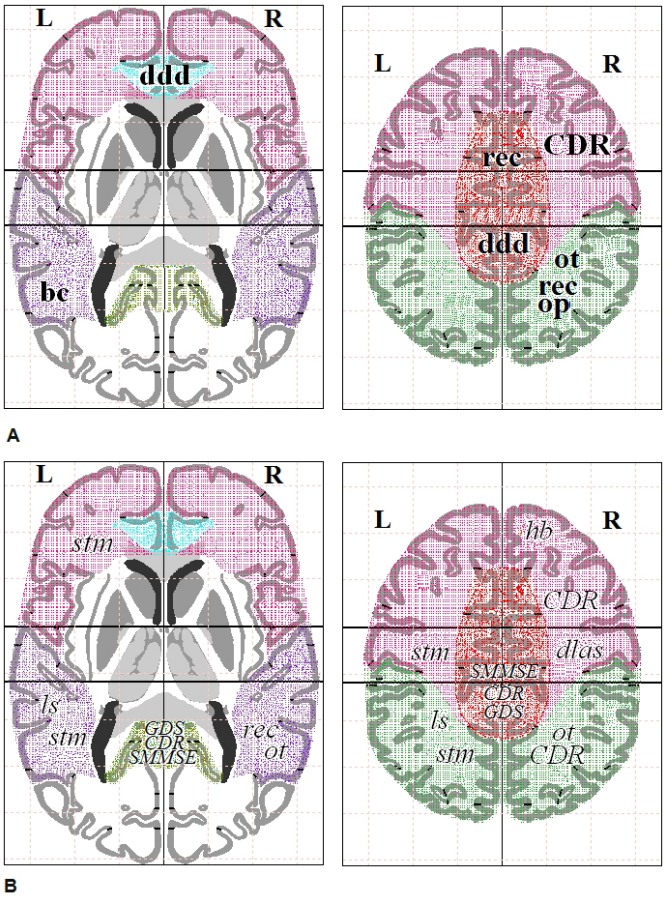

Figure 2a-b: *Global representation of perfusion defects correlated with neuropsychological evaluation in AD (a) and VaD (b) patients according to Talairach applets(17). Standardized mini mental state examination (SMMSE), duration of disease(ddd), recording subscore of SMMSE (rs), clinical dementia rating scale (CDR), backward counting (bc), recording (rec), orientation to time (ot), orientation to place (op), global detoriation scale(GDS), habituations (hb), daily living activity score (dlas), short term memory (stm), language subscores of SMSSE(ls)*

DISCUSSION

In this study clinical variables including detailed neurophyshiatric battery and brain SPECT results has been evaluated. We showed associations between regional perfusion ratios and clinical results in AD and VaD which could not be attributed to patient's personal variables as age, gender, education level, etc.

We have used a detailed and a strong neuropsychological battery to evaluate the localization and degree of cognitive impairment. Neuropsychological screening of AD and VaD patients were identical with each other. SMMSE of control group was statistically different from AD and VaD patients. MMSE is a tool evaluating cognition in severals domains. Dementia severity can be stratified by neuropsychological batteries, but it is not possible to make an accurate differential diagnosis. The reason is that, conditions other than AD may also result in cognitive impairment.

Functional brain imaging is accepted to be useful in the diagnosis of dementing disorders. SPECT or PET can reveal metabolic abnormalities, even in the structurally normal brain. On the other hand, clinical assesment of patients including neuropsychological evaluation is essential to determine the extent of cognitive dysfunction. According to the

results of a study by Tanev et al. most diagnostic changes occurred following family meetings or the functional neuroimaging evaluation by SPECT/PET, with fewer changes after CT/MRI[27].

The primary disadvantage of SPECT imaging is the lower intrinsic spatial resolution when compared to ^{18}F-FDG PET imaging[24]. PET is more sensitive than SPECT in diagnosing early dementia. On the other hand, perfusion SPECT requires an inexpensive, widely available isotope and offers the advantages of lower cost and ease of access.

Brain SPECT imaging provides information on the rCBF and metabolic status of the brain tissue. Based on the principle that rCBF and metabolism are coupled, perfusion SPECT images can be interpreted to reflect regional neuronal activity. A decreased perfusion in the temporoparietal regions of the brain is associated with posterior dementia, such as Alzheimer's type[4].

In our AD group, the altered brain perfusion areas were mostly seen in parietal and temporal regions. However, frontal lobe deficits in conjunction with temporoparietal abnormalities were also detected in patients with severe cognitive impairment. The presence of bilateral temporoparietal hypoperfusion or hypometabolism is a useful biomarker for discriminating AD patients from age-matched controls as well as from vascular dementia and frontotemporal demantia[6]. The temporoparietal abnormality is usually bilateral but can be asymmetrical. Frontal lobe hypoperfusion is also reported in AD patients, but usually in conjunction with temporoparietal abnormalities.

Very early metabolic deficits occur in AD and MCI in the medial portion of the parietal cortex, in the posterior cingulate or retrosplenial region[28]. In our study, the rCBF in the posterior cingulate cortex was significantly lower in AD than control group. The posterior cingulate cortex is the primary and most prominent area of cerebral metabolic and perfusional reduction in AD[11,32].

In VaD, focal asymmetric perfusion abnormalities, patchy CBF abnormality or hypoperfusion corresponding to vascular territories are expected, as it was also observed in our cases. In routine practice, the diagnosis of VaD is normally made by a combination of history, neurologic examination, and MRI. However, the diagnosis of VaD is confounded by the entity of mixed dementia. SPECT has been found to have a role in identifying an Alzheimer's type of perfusion pattern in patients with vascular deficits on CT or MRI and suspected to have mixed dementia[6]. In our study, 4 (25%) patients in VaD group showed patchy CBF abnormalities accompanied with bilateral parietal or temporal hypoperfusion. Mixed dementia were not considered clinically and radiologically in those patients. However SPECT imaging revealed more extensive disease than expected. Comparison of the mean regional perfusion ratios in VaD and control group did not reach to a statistically significant level. This may be because of the small number of cases in VaD group showing different hypoperfusion patterns corresponding to different vascular territories. Additionally, in conditions with patchy perfusion abnormalities, high count pixels and low count pixels normalize each other to give mean value in the regions of interest, which may have resulted in insignificant differences between control and VaD group.

In litrature several studies have focused on different quantitative methods for analysing SPECT data in order to obtain objective and reliable information on abnormalities in CBF[25,31,33]. Staffen W et al.[25] have found a slightly higher agreement between the final diagnosis and the visual findings accompanied by the semiquantitative manual ROI method when compared to pure visual evaluation by an experienced reader. As a part of our

study, we have calculated regional perfusion ratios throughout the brain in order to test the correlation with neurophsychological test battery. Statistical analysis confirmed the association between regional brain perfusion ratios and specific cognitive changes. The reason of negative correlations were because of lower regional brain perfusion ratios and higher neuropsychiatric scores proportional with severity of cognitive impairment. Perfusion defects which were statistically associated with counting, short term memory and language subscores of SMMSE were seen on the left side whereas perfusion defects associated with orientation, habituations and daily living activities were on the right side. In litrature it has been previously documented that, patients with more right-sided deficits suffer from greater visual spatial pathology, while patients with predominantly left-sided deficits show more pathology in speech and language function[9]. A link between calculation and structural integrity of grey and white matter regions in left temporo-parietal cortex were also suggested[29].

Correlation between duration of disease and perfusion defects in limbic and anterior cingulate gyrus which was found in AD group, may be associated to possible behavioural problems which is expected to be more prominent in long term disease. CDR as a good representer of functional daily living capacity was correlated specifically with right frontal area. This correlation showed us an average data about total cognitive performance of executive memory.

The results of this study confirms that perfusion deficits correlate with specific patterns of cognitive abnormalities. Brain SPECT findings integrated with detailed neuropsychological evaluation would increase gain in diagnostic certanity of AD and VaD in clinical practice and help us to understand the degree of cerebral functioning more accurately.

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