ABSTRACT

Background: Alzheimer’s disease (AD) and cerebrovascular disease (CVD) are the most common causes of dementia in the world. For several reasons, however, differential diagnosis of AD versus vascular dementia (VaD) has proved to be difficult. However, their accurate differentiation is of great importance due to different pharmacoeutical strategies which may modify the course of each disease. Objective: The objective of this study is to assess the usefulness of clinical neuropsychological testing, neuro-radiological findings (by MRI) and cerebral blood flow changes (by SPECT) in differentiation of AD and VaD. And to correlate these results with the severity of the dementia, and to find a possible correlation between clinical neuro-psychological deficits and structural and functional abnormalities in MRI and SPECT. Materials and Methods: This study was carried on twenty patients suffering of dementia for more than 2 years duration and were classified into 2 groups, group I included 10 patients having possible AD and group II included 10 patients having possible VaD. Patients of either groups were selected according to the following criteria: DSM-IV for AD, DSM-IV for VaD, Hachinski ischemic scale (HIS), ADDTC scale, NINCDS-ADRDA scale. Patients in this study were subjected to thorough medical, neurological and neurovascular examination, full laboratory investigations, clinical neuro-psychological scales and tests including: CAMCOG, DRS, MMSE Hamilton depression scale, blessed dementia scale, Bristol activities of daily living scale, IDDD and clinical dementia rating (CDR). MRI brain, functional neuro-imaging using SPECT. Results: This study revealed that vascular risk factors (predominantly uncontrolled hypertension) and focal neurological symptoms and signs were mainly a features of VaD and not AD. Patients with AD had significantly more deterioration (P<0.05) in mental and cognitive functions and activities of daily living compared to those with VaD, while those with VaD significantly (P<0.05) were more prone to develop depression and behavioral changes. Bilateral cortical atrophy (especially in the temporo-parietal region) was significantly higher in those with AD (P<0.05) while that of subcortical type (especially in fronto-temporal region) was higher in those with VaD (P<0.05). Multiple brain infarcts is a cardinal feature of VaD and not AD, infarctions were multiple, small, cortical-subcortical mainly in the basal ganglia, thalamus, deep white matter, fronto-temporal areas. Furthermore, white matter hypodensity was significantly higher in these with VaD (P<0.01). SPECT examination revealed that cerebral hypoperfusion was significantly higher (P<0.05) in the posterior parietal, medial temporal regions in patients with AD and higher (P<0.05) in fronto-temporal, basal ganglionic, thalamic areas in patients with VaD. There was a significant positive correlation between the severity of the dementia of either types (assessed by DRS, MMSE, blessed dementia scale and CAMCOG) and cortical involvement and frontal lobe affection in MRI and SPECT examinations. There was a good correlation between the differences in neuropsychological results in both types of dementia
and structural and functional abnormalities observed on MRI and SPECT examination. Neuro-radiological findings recorded by MRI brain examination correlated well with that observed on SPECT examination, however, SPECT demonstrated more brain areas of dysfunction not detected by MRI examination. Conclusion: Clinical neuropsychological testing is a fairly good method for differentiation of the type of dementia (AD versus VaD). However, neuro-imaging and functional imaging add not only a more precise method of differentiation, but also a method to determine the severity of the disease and explain its structural and functional background for these clinical abnormalities. (Egypt J. Neurol. Psychiat. Neurosurg., 2004, 41(1): 35-58).

INTRODUCTION

Alzheimer disease (AD), the most common cause of dementia has been studied extensively, whereas, vascular dementia (VaD), the second most common cause of dementia has been studied sparsely. Unlike AD, it may be possible to arrest the progression of VaD, therefore, the accurate differentiation of VaD from AD is essential. The patterns of impairment of cognition may contribute to this required differentiation. Moreover the diagnostic criteria for each condition refer to neuropsychological deficits that are presumed to be characteristic.

Neuro-imaging is a key procedure in the assessment of dementia especially for differential diagnostic evaluations; recently, interest has focused on neuro-imaging for distinguishing normal aging from pathological conditions and for differentiating the type of dementia such as AD versus VaD.

Single Photon Emission Computerized Tomography (SPECT) is being widely used for cerebral blood flow (CBF) studies. These studies provide unique information for the identification of functional abnormalities relevant to AD. Moreover, SPECT provides a useful method used to differentiate AD from other types of dementia especially VaD.

The sensitivity of SPECT when distinguishing AD from VaD ranged from 43% to 100%. This rather broad distribution has been attributed to difference in SPECT methods, and to the clinical characteristic of the specific population examined.

The diagnostic value of SPECT in the diagnosis of patients with dementia remains unclear. While bilateral temporo-parietal abnormalities are common but not specific for AD, no typical pattern of abnormality was seen in the VaD.

The aim of this study is to assess the usefulness of clinical neuropsychological testing, neuro-radiological findings, and cerebral blood flow changes in differentiating patients with AD and VaD, and to correlate the obtained data with the degree and severity of dementia in each type.

To find possible correlations between neuropsychological deficits recorded clinically, and structural and functional abnormalities detected on neuro-imaging studies (MRI and SPECT of the brain).

PATIENTS AND METHODS

Patients:

* This study was conducted on twenty Egyptian patients suffering of dementia for ≥2 years duration.
* Patients were classified into 2 groups:
  - Group I: included 10 patients (7 males and 3 females) diagnosed as having possible AD. Their ages ranged from 60-81 years with mean age 69.6±2.45 years.
- **Group II**: included 10 patients (6 males and 4 females) diagnosed as having possible vascular dementia. Their ages ranged from 61-81 years with mean age 70.3±2.29 years.

**Patients Selection:**
Patients were selected and diagnosed as having either possible AD or possible VaD according to the following criteria:
1. Diagnostic and statistical manual of mental disorders fourth edition revised (DSM-IV) for diagnosis of Alzheimer’s dementia.
2. Diagnostic and statistical manual of mental disorders fourth edition revised (DSM-IV) for diagnosis of vascular dementia.
3. Hachinski ischemic scale (HIS).
5. National Institute of Neurological and Communicative Disorders and Stroke, the Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA).

**Exclusion Criteria:**
*Excluded from this study:*
All demented patients not fulfilling the criteria for possible AD or possible VaD in the previous selection criteria. Any patients with severe dysphasia, severe hearing or visual impairment.
Patients with disturbed or inconsistent conscious level e.g. delirium.
Patients with concomitant medical or metabolic illness known to affect cognition e.g. hypothyroidism, liver or kidney failure.
Patients with previous history of other significant neurologic or psychiatric disorders known to cause cognitive impairment e.g. major depression, patients with history of significant head trauma with loss of consciousness. Patients with history of taking psychoactive drugs or using drugs known to affect mentality and cognition e.g. anti-cholinergics, anti-epileptics, or anti-psychotics. Patients with a history of alcohol or other substance abuse.
Patients with MRI showing structural brain disease other than brain atrophy, ischemic vascular changes, or white matter change.

**Methods:**
All patients in this study were submitted to the following:
1. Thorough history taking from patients or a near relative using special questionnaire that focuses on vascular risk factors including hypertension, diabetes mellitus. Smoking, ischemic heart disease, previous history of stroke.
2. Thorough medical examination. For detection of vascular risk factors and to exclude other medical causes of cognitive impairment.
3. Thorough neurological examination according to standardized neurological sheet. Neurology Department, Cairo University.
4. Neuro-vascular examination according to standardized neuro-vascular examination sheet. Neurology Department, Cairo University.
5. The following laboratory investigations (for detection of risk factors and to exclude the other causes contributing to cognitive impairment) included:
   a. Complete blood picture.
   b. Fasting and 2 hours post-prandial blood sugar.
   c. Serum urea, creatinine and uric acid.
   d. Complete liver function tests.
   e. Complete lipid profile.
   f. Thyroid function test (free T3, T4, TSH).
6. Clinical neuro-psychological scales and tests:
They included:

a. Scales to assess the mental and cognitive functions:
   - CAMCOG the cognitive examination part of a standardized psychiatric assessment schedule, CAMDEX (the Cambridge examination of mental disorders of the elderly)\(^{16,17}\).
   - Dementia rating scale (DRS)\(^{18}\).
   - Mini-mental state examination test\(^{19}\).

b. Scale to assess the patients’ mood: Hamilton depression scale\(^{20}\).

c. Scales to assess the activities of daily living:
   - Blessed dementia scale of daily living activities\(^{21}\).
   - Bristol activities of daily living scale\(^{22}\).
   - Interview for deterioration in daily living activities in dementia (IDDD)\(^{23}\).

d. Scale to assess the disease severity: Clinical dementia rating (CDR)\(^{24}\).

7. Structural neuro-imaging using MRI brain. MRI brain was done for all patients at the Department of Radiodiagnosis, Cairo University. Parameters studied were: Brain atrophy, brain-infarctions and white matter changes.

8. Functional neuro-imaging using single photon emission computerized tomography (SPECT) to assess the regional CBF. SPECT scans of the brain were performed for all patients at the Department of Nuclear Medicine, Cairo University using Tc99m-Hexamethyl propylenamine (HMPAO) brain SPECT (Tc99 HMPAO SPECT). Two parameters of cerebral blood flow (CBF) were studied.

* Site of the abnormality: Which for ease of data analysis the patterns of CBF abnormality were classified into left and right frontal, parietal, mesial temporal, lateral temporal and occipital areas, in addition to the basal ganglia, thalamus, and cerebellar hemispheres, which were also analyzed for the presence of hypoperfusion.

* Degree of hypoperfusion: As there is a normal variability of the uptake of the radio-active tracer in different parts of the brain, a cut-off point value was determined for each region of the brain, below which pathological hypoperfusion was considered (Table 1).

Table 1. Normal quantitative, SPECT value in different regions of the brain, described as a percentage from the cerebellum uptake.

<table>
<thead>
<tr>
<th>Site</th>
<th>Normal quantitation %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal lobe</td>
<td>87-105</td>
</tr>
<tr>
<td>Parietal lobe</td>
<td>78-90</td>
</tr>
<tr>
<td>Occipital lobe</td>
<td>70-90</td>
</tr>
<tr>
<td>Caudate</td>
<td>85-100</td>
</tr>
<tr>
<td>Thalamus</td>
<td>85-105</td>
</tr>
<tr>
<td>Putamen.</td>
<td>80-105</td>
</tr>
<tr>
<td>Lateral temporal</td>
<td>70-90</td>
</tr>
<tr>
<td>Medial temporal</td>
<td>60-80</td>
</tr>
</tbody>
</table>

In general any activity compared to the cerebellum that is below 60% is considered abnormal\(^{25}\).

**RESULTS**

I. Age and Sex Distribution:
The mean age of patients with AD (group I) was 69.6 years ±2.45 SD (their ages ranged from 60 to 81 years). While that of
patients with VaD was 70.3 years ±2.29 SD (their ages ranged from 61 to 81 years).

Patients with AD were 7 males (70%) and 3 females (30%) while those with VaD were 6 males (60%) and 4 females (40%).

II. Risk Factors:

As shown in Fig. (1) which demonstrates the risk factors in patients with dementia in either group. Comparing the results in both groups revealed, high statistically significant difference (P<0.01) between patients with AD and those with VaD regarding hypertension and ischemic heart disease being much more in those with VaD [hypertension in all patients (100%) and ischemic heart disease in 7 patients (70%) in VaD compared to only 3 patients (30%) for either hypertension or ischemic heart disease in those with AD].

Moreover, all patients with VaD had long standing hypertension (≥10 years duration), both systolic and diastolic, and mostly uncontrolled in 6 patients (60%).

Again, there was a significant difference (P<0.05) regarding cigarette smoking, and cardiac arrhythmia being more in those with VaD.

On the other hand, no significant difference (P>0.05) between the 2 groups of patients (AD and VaD) was observed regarding other risk factors studied (DM, hyperlipidemia, and hyperuricemia). Although diabetic patients were more in those with VaD while those with hyperuricemia were more in those with AD.

III. Clinical Neurological Findings:

Clinical neurological examination findings as shown in table (2) revealed that, patients with VaD had much more neurological deficits on examination than those with AD (except for the presence of primitive reflexes being more in those with AD).

High statistically significant difference (P<0.01) was observed regarding the presence of motor deficits, gait disturbance, speech disturbance, cranial nerves involvement, incoordination and sensory deficits (mainly of cortical type) and a significant difference (P<0.05) regarding the presence of extrapyramidal manifestations (mainly rigidity, flexion attitude, abnormal short gait) being more in those with VaD.

On the other hand, no significant difference was found regarding sphincteric troubles (although being more in those with VaD mainly in the form of precipitancy) and presence of primitive reflexes (being more in patients with AD).

IV. Neuro-Psychological Examination and Scaling of Dementia:

Table (3) demonstrates the results of comparison between the 2 groups of patients (AD and VaD) regarding the mean of scores different neuropsychiological scales and tests used in this study.

Comparing the cognitive functions and mental deficits revealed that the deterioration of mental functions is much more significantly affected in those with AD than with VaD (P<0.01 for CAMCOG and P<0.05 for MMSE and DRS). Moreover, aspects being mostly affected in AD patients were orientation, language, memory especially recent and recall memory, abstract thinking and praxia, while in those with VaD, were executive functions mainly verbal memory, verbal fluency speech, attention, slow mentation, praxia with less severe memory affection.

The activities of daily living were much more significantly disturbed (P<0.05) in those with AD than with VaD, also patients with AD become dependent earlier than those with VaD.
Regarding the Hamilton depression scale, the results revealed that patients with VaD were significantly (P<0.05) more prone to have depression than those with AD.

The severity of the disease was assessed using the clinical dementia rating scale (mainly) and supported by the mean score of MMSE, CAMCOG scale and blessed daily living activities scale and demonstrated in table (4). Two patients (20%) with AD were categorized as having mild to moderate dementia while 8 patients (80%) as having moderate to severe dementia. On the other hand, in patients with VaD these figures were 4 patients (40%) and 6 patients (60%) respectively.

V. Neuro-Radiological Results (MRI findings):

The neuro-radiological findings studied on MRI examination were: (a) brain atrophy, (b) brain infarctions and (c) white matter changes.

Regarding brain atrophy all patients (100%) of either group had a variable degree of bilateral brain atrophy.

Patients with AD dementia had cortical atrophy (only) in 8 patients (80%) and mixed cortical-subcortical in 2 patients (20%) while atrophy was cortical (only) in 3 patients (30%) of those with VaD, subcortical (only) in 5 patients (50%) and mixed cortical-subcortical in 2 patients (20%). So cortical atrophy was significantly higher in those with AD (P<0.01) while subcortical atrophy was significantly higher in those with VaD (P<0.01) (Fig. 2). Moreover, temporoparietal atrophy was significantly higher in those with AD (7 patients 70%) while fronto-temporal atrophy was significantly higher in those with VaD (7 patients 70%). Occipital lobe atrophy and cerebellar atrophy were found only in patients with VaD (2 patients and 3 patients respectively) and not in patients with AD (Fig. 3).

The second radiological finding examined was brain infarctions, a finding which was found in all patients with VaD (100%) and only in 2 patients (20%) with AD, a difference which reached a highly significant statistical value (P<0.01).

Infarctions of patients with VaD were mainly cortical-subcortical (mixed) in 7 patients (70%), cortical only in one patient (10%) and subcortical in 2 patients (20%) (Fig. 4), while that of patients of AD were subcortical.

All patients with VaD had bilateral multiple brain infarctions which were small in size in 70% of patients, and mixed small and large in 30% of patients, while those with AD had their infarctions small and single.

In VaD patients, deep periventricular, basal ganglionic, thalamic infarctions each was found in 9 patients (90%), 6 patients (60%) had their infarctions in the fronto-temporal area, 3 patients (30%) in the temporo-parietal area, 3 patients (30%) in the occipital area, 2 patients (20%) had brain stem infarctions and another 2 patients (20%) had cerebellar infarctions (Fig. 5).

The third finding studied was the white matter hypodensity (leuco-encephalopathy), a bilateral nearly symmetrical radiological finding was found in all patients (100%) with VaD and only in 3 patients with AD, a difference which reached a highly significant value (P<0.01).

VI. MRI Findings and Severity of the Dementia:

Comparing patients with mild to moderate VaD to those with moderate to severe dementia, regarding the radiological
findings revealed that: those with more severe degree of dementia had significantly a higher degree of atrophy which was exclusively fronto-temporal and mostly with cortical involvement either alone or with subcortical involvement in addition). Again, those with more severe degree of VaD showed significantly higher bilateral mixed cortical-subcortical or cortical (only) brain infarctions, especially of the fronto-temporal area, especially on left side.

On the other hand, the same comparison for patients with AD revealed that, the more severe degree of dementia was significantly associated with high degree of atrophy which was exclusively cortical and mainly affecting the temporo-parietal area bilaterally.

In both group of patients it was observed that, frontal lobe involvement either by brain atrophy or brain infarctions is significantly associated with more severe degree of dementia, more worsen scores of cognitive functions and daily living activities.

VII. SPECT Results:
All patients (100%) of both groups of patients (AD and VaD) had bilateral multiple area of hypoperfusion on SPECT examination.

A. Site of hypoperfusion: (Table 5)
Patients with AD were affected in the following frequency: Medial temporal in 6 patients (60%), posterior parietal in 5 patients (50%) lateral temporal in 3 patients (30%). Frontal, anterior parietal, basal ganglionic each in 2 patients (20%). Cerebellum and thalamus each in only one patient (10%).

While patients with VaD were affected in the following frequency: bilateral patchy deep periventricular areas of hypoperfusion in all patients (100%). Basal ganglionic in 8 patients (80%), thalamic in 7 patients (70%), frontal in 5 patients (50%), lateral temporal and anterior parietal each in 4 patients (40%), occipital in 3 patients (30%), and posterior parietal and medial temporal each in 2 patients (20%), lastly cerebellar hypoperfusion was noted in 2 patients (20%). Comparing the results of both groups revealed that: SPECT hypoperfusion is significantly higher (P<0.05) in posterior-parietal, medial temporal regions for patients with AD and higher in frontal, anterior parietal, occipital areas, basal ganglia, and thalamus in those having VaD.

B. Degree of hypoperfusion: (Table 6)
Patients with AD showed maximum degree of affection in the medial temporal area, posterior-parietal area followed by frontal area. Whereas; patients with VaD showed their maximum degree of abnormality in the frontal area especially on left side, ant-parietal area, deep white matter especially of fronto-parietal area, basal ganglionic, and thalamic regions.

VIII. SPECT Findings and Severity of the Dementia:
Comparing the site and degree of cerebral hypoperfusion in SPECT examination in both groups in those having mild to moderate dementia to those having moderate to severe dementia revealed that: patients with more severe AD had more affection of medial temporal and posterior parietal areas bilaterally, while in patients of VaD, no characteristic pattern was observed to be associated with the severity of the dementia apart from the higher incidence of frontal lobe involvement (either cortical or cortical-subcortical) especially on left side.
Table 2. Clinical neurological findings in both groups of patients with dementia.

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Group I (AD) (10 patients)</th>
<th>Group II (VaD) (10 patients)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Speech disturbance</td>
<td>3</td>
<td>30</td>
<td>7</td>
</tr>
<tr>
<td>Cranial nerves abnormalities</td>
<td>1</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Motor weakness</td>
<td>2</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Incoordination</td>
<td>2</td>
<td>20</td>
<td>7</td>
</tr>
<tr>
<td>Extrapyramidal manifestations</td>
<td>2</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Gait disturbance</td>
<td>4</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Sensory deficit</td>
<td>1</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Sphincter disturbance</td>
<td>5</td>
<td>50</td>
<td>7</td>
</tr>
<tr>
<td>Primitive reflexes</td>
<td>10</td>
<td>100</td>
<td>8</td>
</tr>
</tbody>
</table>

*Significant **Highly significant

Table 3. Results of neuro-psychological testes and scales in both groups with dementia

<table>
<thead>
<tr>
<th>Neuropsychological tests and scales</th>
<th>Group I (patients with AD)</th>
<th>Group II (patients with VaD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ±SD</td>
<td>Range</td>
</tr>
<tr>
<td>I. Cognitive and mental functions:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. MMSE</td>
<td>12-16</td>
<td>14.3±0.44</td>
<td>17-21</td>
</tr>
<tr>
<td>2. CAMCOG</td>
<td>41-53</td>
<td>47.7±1.42</td>
<td>61-77</td>
</tr>
<tr>
<td>3. D. rating scale</td>
<td>9-17</td>
<td>12.3±1.59</td>
<td>1-20</td>
</tr>
<tr>
<td>II. Activity of daily living:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Blessed D.scale</td>
<td>16-19</td>
<td>17.5±3.13</td>
<td>11-17</td>
</tr>
<tr>
<td>2. Bristol</td>
<td>29-44</td>
<td>36.5±1.48</td>
<td>21-40</td>
</tr>
<tr>
<td>3. IDDD</td>
<td>52-73</td>
<td>61.3±2.53</td>
<td>33-67</td>
</tr>
<tr>
<td>III. Depression:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamilton depression scale</td>
<td>20-32</td>
<td>27.1±1.23</td>
<td>22-47</td>
</tr>
</tbody>
</table>

* Significant

Table 4. Grading of the disease severity using clinical dementia rating scale.

<table>
<thead>
<tr>
<th>Grading of dementia</th>
<th>Group I (patients with AD)</th>
<th>Group II (patients with VaD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Mild to moderate</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Moderate to severe</td>
<td>8</td>
<td>80</td>
</tr>
</tbody>
</table>
Table 5. Sites of hypoperfusion on SPECT examination in both groups of patients with dementia

<table>
<thead>
<tr>
<th>Hypoperfusion on SPECT exam</th>
<th>Group I (patients with AD)</th>
<th>Group II (patients with VaD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Positive Site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal</td>
<td>2</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Anterior-parietal</td>
<td>2</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Posterior parietal</td>
<td>5</td>
<td>50</td>
<td>2</td>
</tr>
<tr>
<td>Medial temporal</td>
<td>6</td>
<td>60</td>
<td>2</td>
</tr>
<tr>
<td>Lateral temporal</td>
<td>3</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>Occipital</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Thalamic</td>
<td>1</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>B.G</td>
<td>2</td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>1</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Number:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patchy</td>
<td>3</td>
<td>30</td>
<td>10</td>
</tr>
<tr>
<td>Single</td>
<td>7</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>Bilaterality</td>
<td>10</td>
<td>100</td>
<td>10</td>
</tr>
</tbody>
</table>

*Significant **Highly significant

Table 6. Results of degree of hypoperfusion on SPECT examination of both groups of dementia.

<table>
<thead>
<tr>
<th>Sites of hypoperfusion</th>
<th>Group I (patients with AD) Mean ±SD</th>
<th>Group II (patients with VaD) Mean ±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal</td>
<td>85.3±1.23</td>
<td>69.7±1.07</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Anterior parietal</td>
<td>80.5±0.27</td>
<td>71.3±0.87</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Posterior parietal</td>
<td>65.8±1.37</td>
<td>79.2±0.79</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Medial temporal</td>
<td>51.2±1.72</td>
<td>69.3±0.84</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Lateral temporal</td>
<td>78.3±0.72</td>
<td>77.5±0.82</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Occipital</td>
<td>81.2±0.92</td>
<td>76.3±0.87</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Thalamus</td>
<td>91.2±0.37</td>
<td>69.7±1.27</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>90.3±0.42</td>
<td>71.8±1.35</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>95.2±0.37</td>
<td>91.3±0.78</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

*Significant
Fig. (1): Risk factors in patients with dementia (VaD and AD)

Fig. (2): Types of brain atrophy in patients with dementia.
T.P: Temporo-parietal, F.T: Fronto-temporal

Fig. (3): Sites of brain atrophy in patients with dementia

Fig. (4): Depth of infarctions in patients with VaD.

Fig. (5): Sites of the infarctions in patients with VaD.
Fig. (6): Brain MRI showing bilateral temporo-parietal atrophy.

Fig. (7): Brain SPECT showing bilateral medial temporal and posterior parietal areas of hypoperfusion.

Figs. (6 and 7): MRI and SPECT of a patient with AD.
Fig. (8): Brain MRI showing bilateral periventricular W.M ischemic changes.

Fig. (9): Brain SPECT showing bilateral areas of hypoperfusion of patchy distribution.

Figs. (8 and 9): MRI and SPECT of a patient with VaD.
Alzheimer’s disease (AD) and cerebrovascular disease (CVD) are the most common causes of dementia in the world. For several reasons, however, differential diagnosis of AD versus vascular dementia (VaD) has proved to be difficult. However, their accurate differentiation is of great importance, due to different pharmacoeutical strategies which may modify the course of each disease.

In this study we try to assess the utility of neurological testing, MRI findings and SPECT findings to differentiate dementia due to AD and that is due to VaD and to throw light on the possible correlation between these findings in both types of dementia.

This study revealed a significantly higher vascular risk factors in patients with VaD compared to those with AD, and these findings were supported by the results of many studies, who reported that many atherogenic factors seem to be a risk for developing VaD, namely hypertension, IHD, cardiac arrhythmia, heart failure, DM, cigarette smoking, obesity and hypercholesterolemia.

One of the most important risk factors for the development of VaD was hypertension, which was present in all patients with VaD. Moreover, all patients had both systolic and diastolic hypertension for more than 10 years duration and most of them (6 patients 60%) were uncontrolled or irregularly controlled. These findings denote the importance of uncontrolled long standing hypertension as a risk factor for developing VaD. Again, this was in consistent with the reports of many studies.

On the other hand, different vascular factors are not significantly related to the development of AD. However, it is reported that factors such as family history, sex, serious head injury, smoking, cholesterol level and estrogen may modify the APOE-related risk for AD. Moreover, Hoffman et al. and Skoog have noted synergy between E4 and vascular risk factors or multifocal white matter vascular lesions in increasing the risk of AD.

The clinical neurological examination (excluding mental state examination) is very important item for differentiation of AD from VaD. This study revealed that patients with VaD had significantly much more focal neurological deficits than those with AD. This was consistent with that reported by Del Ser et al. who observed that in VaD the dysfunction is in one or more cognitive domains with patchy distribution of deficits and stepwise deterioration course. Focal neurological symptoms and signs are frequently present on examination including weakness of an extremity, exaggeration of deep tendon reflexes, an extensor plantar response and gait abnormalities.

On the other hand, neurological examination of patients with AD is usually normal. Commonly associated features include presence of primitive reflexes, impaired cortical sensation, and less common features as, extrapyramidal signs, gait disturbance and Myoclonus.

The previously reported data were in accordance with the results of other studies who reported that focal neurological deficits is a cardinal features of vascular and mixed dementia while this is not the case for AD.

The present study revealed that mental and cognitive functions were much more significantly affected in patients with AD compared to those with VaD. Furthermore, most aspects being affected in AD disease patients were mainly in memory (either verbal
or non-verbal), especially long-term memory and language, abstract thinking and orientation with no significant deficits in perception, construction, attention or executive functions, while those with VaD had greater defects in executive functions, attention, speech, slow mentation with relative preservation of long term memory, these findings were in accordance with many reports.

Moreover, Roman et al. and Tiernery et al. observed that cognitive deficits in patients with VaD are multifocal and highly variable (depending on the size and location of vascular brain injury), and therefore more varied than generally seen in AD. Memory deficits may be not as marked as AD and discrepancies between verbal and non-verbal elements, or visuospatial dysfunction, dysphasia, cognitive slowing and impaired executive function (impairment of frontal lobe functions) are usually more seen in VaD than AD, on the other hand deficits in AD is attributed to selective vulnerability of medial temporal lobe structures to neuro-fibrillatory degeneration.

On the other hand, the two groups of patients did not differ significantly on tests of language, constructional abilities, memory registration, conceptual functions and attention.

In this study patients with AD were significantly more handicapped and became dependent earlier than those with VaD, as proved by the results of scales for daily living activities used (Blessed demenetia scale, Bristol daily activities scale and IDDD). This was supported by the observations of many authors.

Patients with VaD were significantly more prone to develop depression than those with AD, a finding which was consistent with the reports of many studies who observed that affective symptoms (such as depression), psychotic symptoms and behavioral alternations such as delusions, agitation and hallucinations are common complications of VaD.

Furthermore, other studies reported that depressive disorders including major depression and other less severe but clinically significant depression are common co-morbid components or complications of VaD. Moreover, depression may be premonitory sign for VaD.

The high prevalence of depression in those having VaD may be explained by the relative preservation of self-awareness and insight in those having VaD for relatively longer time than those with AD.

Not surprising that, those with moderate to severe grade of dementia of either types (AD and VaD) suffered more significantly from deterioration of cognitive functions and became more dependent and handicapped. Conversely with progress of the disease the incidence and severity of depression and affective symptoms became less evident while the psychotic and behavioral symptoms became more clear.

Regarding the neuroradiological findings, this study revealed that bilateral cortical mainly temporo-parietal atrophy is a prerequisite for the development of AD. On the other hand only 50% of patients with VaD had bilateral cortical (mainly fronto-temporal) atrophy and the other 50% had exclusively subcortical atrophy. The previously reported findings were in accordance with that of many studies.

As mentioned above bilateral cortical atrophy is an essential pre-requisite for the development of AD. On the other hand, bilateral multiple brain infarctions is essential for the diagnosis of VaD which in this study were mainly cortical-sub-cortical, and mainly in the following sites basal ganglia, thalamus, fronto-temporal and tempo-parietal regions.
These findings were supported by reports of various studies.\textsuperscript{27-32}

Again, cortical involvement is the most important feature for development of dementia of the either types (bilateral cortical atrophy in 100% of patients with AD and 50% of those with VaD, bilateral cortical infarctions in 80% of patients with VaD).\textsuperscript{38-40,42,43}

Another important finding is the involvement of temporal lobe in most of patients of both types (in both groups) either by atrophy or infarctions, this goes with Tatemichi et al.\textsuperscript{49} who reported the importance of cortical involvement especially the temporal lobe for the development of AD or VaD.\textsuperscript{42-44}

White matter ischemic changes were common radiological findings in patients with VaD (100% of patients) and only infrequently found in those with AD (30% of patients) a finding which was supported by Boon et al.\textsuperscript{50} who reported that in VaD periventricle white matter changes were 11.6 times greater than in AD and 3.5 times greater than in healthy people, and subcortical WMLs were 2.6 and 13.5 times respectively.

Kantarci and Juck\textsuperscript{51} reported that severe temporal atrophy, hypo-intensities involving the hippo-campal or insular cortex and gyral hypo-intensity bands are more frequently noted in AD. Basal ganglionic/thalamic hyper-intensities, thromboembolic infarctions, confluent white matter and irregular periventricular hyper-intensity are more common in VaD. These were in accordance with the study results.

Although Tatemichi et al.\textsuperscript{49} reported the importance of cortical involvement for the development of dementia (an observation which well documented in this study), Kertesz et al.\textsuperscript{52} and Tatemichiet al.\textsuperscript{53} reported that subcortical sites especially grey matter nuclei or thalamus, or white matter pathways between association areas e.g. periventricular zone, centrum semiioval or between subcortical-cortical regions of the limbic system lead to disconnection syndrome contributing to various cognitive disturbances and various neurological deficits on clinical examination. This subcortical involvement was found in 90% of patients with VaD.

The radiological findings in patients with VaD were supported by many authors\textsuperscript{5,15,29,49,52} who suggested that the cumulative burden results from the number of such lesions with multiple strategically located infarcts causing cognitive decline. The total volume of such lesions or both characteristics reaching a critical threshold overcoming the brain compensatory capacities.

Functional imaging of the brain using SPECT revealed typical hypoperfusion in bilateral medial-temporal, posterior-parietal and occasionally frontal regions in patients with AD. On the other hand, bilateral periventricular, basal ganglionic, thalamic and frontal regions are the mostly affected regions in those with VaD.

The previous results were in accordance with the SPECT criteria reported by Talbot et al.\textsuperscript{8}. For differentiating AD form VaD and these criteria were bilateral posterior CBF abnormality or bilateral posterior plus unilateral anterior CBF abnormality provides support for the diagnosis of AD. By contrast, bilateral anterior CBF abnormalities or bilateral anterior CBF plus unilateral posterior CBF abnormalities or patchy CBF changes provide support for diagnosis of VaD. Unilateral posterior, unilateral anterior, unilateral anterior plus unilateral posterior, generalized CBF abnormalities and normal CBF pattern fail to differentiate either disorders (VaD and AD).

Many studies\textsuperscript{6,8,9,54-56} reported that bilateral hypo-perfusion in the association
cortex of the parietal lobes and the posterior temporal regions (with or without frontal lobe perfusion defect) is considered to be the characteristic SPECT findings in AD. A finding which was consistent with the study results.

Our SPECT findings in patients with AD confirm the currently accepted observation of a bilateral (either symmetric or asymmetric) hypoperfusion of the posterior temporal and parietal areas, as the most typical SPECT picture in patients with AD with widespread cognitive deterioration.\(^{42,43}\) Worthnoting that in AD, brain damage spreads from the parieto-temporal association cortex to the occipital and frontal cortex according to the progression of the disease severity.

On the other hand, no typical pattern of abnormalities was seen in patients with VaD, as SPECT findings varied greatly according to the site and degree of vascular brain injury.\(^{12,55,57,58}\)

**Correlation between MRI findings and SPECT findings:**

The study results revealed a good significant correlation between the anatomic disturbances (MRI findings) and functional abnormality (SPECT findings). Cortical affection (either by atrophy or brain ischemic changes), and temporo-parietal region affection in AD patients, fronto-temporal region, and deep gray matter substances and white matter in VaD were nearly consistent in both neuro-imaging and functional imaging. However, SPECT can demonstrate a further areas not detected by neuro-imaging as basal ganglionic, and thalamic affection in some patients with AD. Moreover, SPECT can provide a more clear idea about degree of functional disturbances compared to MRI.

This was supported by the report of P. Velakoulis and Lloyd\(^{58}\) who stated that the pattern of SPECT abnormality was concordant with structural neuro-imaging in 65% of patients and neuro-psychological testing in 82% of patients. These were supported by many studies.\(^{59-68}\)

**Correlation between neuropsychological findings and neuro-imaging findings (structural and functional) (MRI and SPECT):**

Usually there is a close relation between neuropsychological profiles and neuro-radiologic findings and patterns of regional brain dysfunction shown by SPECT.\(^{42,62,63}\)

Firstly, these results emphasis on the importance of cortical involvement (with variable degree of subcortical involvement) for the occurrence of dementia. A finding which correlated well with the cardinal neuropsychological manifestation of dementia of either type, which was a result of disturbance in cortical functions or its subcortical connections especially memory and executive functions.

This study reported the importance of involvement of temporal lobe structures in either type (in addition to parietal in AD and frontal in VaD). So that demonstrating the importance of temporal lobe regions for processing of memory.

**Reasons for differences in neuropsychological tests performance:**

Looi and Sachdev\(^{69}\) reported that, to understand the pathogenesis of these differences in the two dementia syndrome, one must examine their neuro-pathologic basis. Memory is supported by multiple neural systems with particular involvement of the medial temporal and diencephalic structures.\(^{39,40,67-74}\)

In AD the neuro-pathologic lesions impact directly and early on structures closely associated with memory.\(^{74,75}\) It has been suggested that the initial episodic memory impairment in AD is due to trans-entorhinal neuropathology (causing disconnection of the
hippocampus). This is followed by semantic memory deficits reflecting the spread of the pathology to the adjacent temporal neocortex\textsuperscript{66,67,76,77}. So, a mesial temporal localization of brain impairment was already reported by studies using MRI and SPECT in patients with AD\textsuperscript{78}.

It is not surprising that patients with AD in this study were characterized by deficits in recognition memory. This pattern is well established in the AD literature. Poor recognition memory is considered to reflect deficits in storage caused by deficient consolidation of new memory traces\textsuperscript{26,79}. This, in turn is often linked to the degeneration of the mesial temporal areas namely the hippocampus, and amygdala. These areas are highly vulnerable to neuro-fibrillary degeneration one of the classic neuropathological hallmarks of AD\textsuperscript{80,81}. Thus poor recognition memory among patients with AD is likely due to neuro-fibrillary degeneration in the mesial temporal lobes including the hippocampus.

In contrast, verbal memory may be relatively spared in VaD due to the heterogeneity of the neuropathology resulting in lesser impact on widely distributed memory system and the frequent sparing of medial temporal lobe structures. The relative excess of deficits ascribed to pre-frontal lobe function in VaD may be explained by the frequent presence of lesions in structures that comprise the frontal subcortical circuits.

These frontal subcortical circuits typically consist of neuronal connections from the frontal cortex to basal ganglia, down to the thalamus with feedback flow from the thalamus to the frontal cortex\textsuperscript{82,84}. So dysfunction can occur due to damage to any part of the circuit. The circuits disrupted in VaD include: The dorsolateral prefrontal circuit mediating executive functions, orbito-frontal circuit mediating emotional lability and the anterior cingulate circuit responsible for motivation and initiation\textsuperscript{83,84}. Thereby explains the excess frontal executive dysfunction in VaD observed in this study. Furthermore, our results were supported by many authors\textsuperscript{84-89} who reported that correlated imaging studies lend support to the conceptualization of VaD as being characterized by a greater degree of frontal lobe dysfunction than in AD of the same severity.

Subcortical infarcts, because of the characteristics of cerebral-vasculature, tend to occur within cortico-striato-thalamo-cortical anatomical loops that support the functioning of pre-frontal cortex. So dementia may follow in part due to generalized impact of the loss of cognitive regulatory functions of the frontal lobe\textsuperscript{90,91}. This suggestion was supported by: empirical description of cerebral vasculature\textsuperscript{92}, radiological studies showing that lacune predominantly occur in the thalamus, basal ganglia, frontal white matter (all of which are important components of frontal-subcortical circuits) and by functional studies using SPECT which demonstrated that hypoperfusion was more frequent in that areas\textsuperscript{93-95}. Lastly this was supported by neuro-psychological studies of VaD that shows the predominance of symptoms associated with frontal lobe dysfunctions\textsuperscript{44,87,91}. Patients with subcortical ischemic vascular disease tend to show greater impairment in executive function and relatively better preservation of recognition memory\textsuperscript{28}.

Moreover Obrien et al.\textsuperscript{62} reported that functional imaging studies of ischemic VaD are considerably less uniform in their findings than are the studies on AD\textsuperscript{90-94}. However, recently more consistent findings have been emerged, and these studies support the idea that subcortical infarcts impair cognition through their effects on the cortex, and
suggest that basal ganglia and prefrontal cortex are especially hypoactive in VaD. The previous observations support our SPECT data in VaD.\textsuperscript{63,70,96}.

White matter ischemic changes which were observed predominantly in VaD were correlated with the severity of apathy, decreased affect, depression, and social withdrawal in many studies.\textsuperscript{96}

Although the specific pathophysiology of apathy, depression or psychomotor slowing is unknown, recent studies suggest that these symptoms, may be due to pathological changes in the frontal-subcortical pathway, and frontal lobe perfusion deficits and dysfunction of dopaminergic serotenergic and nor-adrenergic neuro-transmission.\textsuperscript{96,97}

Relation between neuro-anatomical imaging, functional imaging and severity of dementia:

This study revealed that those with more severe type of dementia of either types had a more severe involvement of the temporo-parietal area in those with AD and deep periventricular area (especially of prefrontal area) and thalamic area in VaD. Furthermore, frontal lobe involvement of both types is associated with more severe types of dementia. A result which was supported by many authors who emphasis the importance of frontal lobe involvement as a predictor for the disease severity.\textsuperscript{96,98}

REFERENCES


الملخص العربي
التقييم الإكلينيكي والتقييم العصبي السينولوجي الإكلينيكي وأشعة الدماغ المغناطيسية على المخ والأوعية بالنظارات المقطعة أحادية الفوتون على المخ في العنة الناتج عن مرض الزهايمر والنتائج عن أمراض الأوعية الدموية المخية

يعد مرض الزهايمر وآرامات الأوعية الدموية المخية من أهم أسباب الوفاة في العالم، ولكن لأسباب عديدة توجد هناك صعوبة في التعرف عليها ونؤمن أن هذه التعرف مهمة لاتخاذ طرق العلاج فيما بعد.

وقد أجريت هذه الدراسة لتحديد أية التغييرات في التقييم الإكلينيكي والعصبي السينولوجي الإكلينيكي والأوعية بالنارين المغناطيسية للمخ ودراسة تغييرات الإمداد الدموي للمخ باستخدام الأشعة المقطعة بالأشعة السينوجية في المريض缕缕 التقييم الناتج عن مرض الزهايمر وذلك النتائج عن أمراض الأوعية الدموية المخية، والمساعدة في إجراء علاقة بين هذه التغييرات مع درجة المرض، وبناء علاقة بين التغييرات في الاختبارات السينولوجية الإكلينيكي وأشعة الدماغ المغناطيسية في المريض缕缕 النتائج المقطعة بالأشعة السينوجية الناتجة عن المريض缕缕 الصدر.

تمت هذه الدراسة على 20 مريضاً مصري عامون من مرض الزهايمر ونظام (2) تفقد أيضاً عشرة مرضى عامون من مرضى العنة الناتج عن أمراض الأوعية الدموية المخية، وفحص المرضى في المجامع المشابهة الإكلينيكي وأجريت لهم الاختبارات والمقياس السينولوجي الإكلينيكي وأجريت لهم الاختبارات المعملية المشابهة، وعمل نتائج الرين المغناطيسية على المخ والأوعية المقطعة بالنظارات المقطعة البئرة على المخ، وبالمصاب عادة المدة لأشعة الفوتون على المخ.

وقد أظهرت نتائج البحث التالي: عوامل الخطر الموروث لحدوث العنة وخاصة ارتفاع ضغط الدم والإضطراب الموضوعي العصبي في موقيت العنة الناتج عن أمراض الأوعية الدموية المخية ولدي العنة الناتج عن مرض الزهايمر، مرضى العنة الناتج عن مرض الزهايمر عامون من تدوير حالة الوعي المعرفي بحيث تدور في حالة الوعي المعرفي أثر

من مرضى العنة الناتج عن أمراض الأوعية الدموية المخية وأن مرضى عني اضطراب الأوعية الدموية عامون أكثر من الاكتتاب واضطراب الصراف، مرضى العنة الناتج عن مرض الزهايمر عامون من تدوير القشرة المخية وخاصة في المنطقة السينولوجية، وهم يعاني مرضى العنة الناتج عن أمراض الأوعية الدموية من ضمور القشرة المخية وخاصة في المنطقة السينولوجية، وذلك بفضل الاستخدام المتعدد، وكذلك تغيرات الماء البشرية في عامة من أعمائط مرضى العنة الناتج عن أمراض الأوعية الدموية المخية. فقص الإدماد الدموي في المنطقة الجدارية الخفيفة والسينولوجية الداخلية أم مظاهر العنة الناتج عن مرض الزهايمر في الأوعية المقطعة بالإشارة المقطعة أحادية الفوتون بينما نقص الإدماد الدموي في المنطقة الأدمادالية الصغيرة والخلايا المئوية ومثلة المدة لم يظهر العنة الناتج عن أمراض الأوعية الدموية المخية.

تترتب درجة المرض بالتكييف الخفيف في المخ وتأثير الفص الأيسر من المخ، وتفحص عادة تجريد بين المخ. وعندما تتشكل التغييرات في نتائج التقييم العصبي السينولوجي الإكلينيكي في مرضى العنة (نوعية) والتغييرات المتعددة للمريضه (الشائبة بالأوعية بالرطوبة المغناطيسي على المخ والوظيفية) (الشائبة بالأوعية المقطعة بالنظارات المقطعة أحادية الفوتون على المخ، وكذلك هذه التغييرات بين الرياح والمتوسطة في المريض缕缕 الإمداد الدمويوسطي بالأشعة المقطعة أحادية الفوتون على المخ في مرضى العنة الناتج عن أمراض الأوعية الدموية المخية.

ومن هنا يتضح أن اختبارات المقياس السينولوجي الإكلينيكي هي وسيلة جيدة للتكشف عن أوقات العنة، ولكن الفحص يمكن أن تكون في النتائج بأوقات العنة بالأشعة الرئوية على المخ وأشعة الدماغ المغناطيسية تجاه التغييرات المقطعة أحادية الفوتون، كما أنها تنشر الأساس العضلي والوظيفي للاختبارات السينولوجية الإكلينيكي والسينولوجي.