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Brain Computerised Tomographic Findings In Elderly Nigerians With Alzheimer's Disease

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ABSTRACT

The Brain C/T Scan of 56 Elderly Nigerians made up of 20 cases of clinically diagnosed Dementia (Study Group) and 36 Non-Demented cases that are considered free of significant Cognitive impairment (Control Group), were evaluated. The subjects were selected and categorized based on their performance on the screening tests, which consist of both a screening stage and a Clinical assessment stage.

The Study group recorded a significant smaller Brain (142.93+/- 91.6) than the Control group (148.6+/-12.7), and is associated with larger Ventricular sizes. No statistically significant Sex difference was established in both Clinical groups studied. The expected Linear Age relationship with Brain size was found to be less applicable in the Dementia study group, which is attributed to the pathology of the Alzheimer's disease (AD).

Cortical Atrophy was the predominant Brain C/T changes found in both Clinical groups studied, but they are more pronounced, though not statistically significant, in the Dementia group. The statistically significant lower MMSE (11.6+/-5) recorded in the Dementia group shows that a significant relationship exist between level of cognitive deterioration and C/T indices of Brain Atrophy.

Keywords: Brain, Dementia, Cognitive, Alzheimer's, Atrophy.

INTRODUCTION:

The role of neuro-imaging in the differential diagnosis of dementia has been up until recently, mainly for excluding non-degenerative causes such as neoplasm, subdural haematoma and cerebro-vascular disorders.

The accuracy of the clinical diagnosis of degenerative dementia, particularly of Alzheimer's disease (AD), in the living person is most often uncertain. Attempts to distinguish between AD, normal ageing and other causes of dementia have been made through the quantitative assessment of Ventricular sizes, CSF spaces and Cortical Atrophy, using subjective and objective ratings on Computerized Tomography (CT) examinations. LeMay et al [8] and Pearlson G.D et al[12] showed that Medial Temporal CT measures (Suprasellar Cistern ratio) can best distinguish AD subjects from controls. Radiological changes on both CT and Magnetic Resonance imaging (MRI) have consequently become an important compliment to clinical evaluation in the diagnosis of dementia. Recent studies have shown that global and regional brain atrophy is a sensitive radiological marker of AD on CT and MRI [16,17,18]

In view of the cultural and educational influences on the clinical indices used in the diagnosis of dementia, the validity of cross-cultural comparisons of the epidemiology of AD would benefit from objective makers of brain pathology. When such comparisons are made on data derived from living subjects, radiological measures may be a powerful compliment to clinical assessments by enhancing the validity of the later.

The Ibadan-Indianapolis comparative study of dementias is a cross-national project aimed at determining differences in the occurrence of AD in elderly African Americans and in elderly Yoruba Africans residing in Nigeria. An important

component of the study is the radiological evaluation of participants at the two sites. This report is based on data derived from CT investigations conducted on the Nigerian subjects with and without clinically diagnosed AD during the prevalence phase of the study.

MATERIALS AND METHOD

The report is based on data derived from a community-based study of dementia in Nigerians aged 65 years and over, residing in Idikan ward in the city of Ibadan. A full account of the study is given elsewhere[10]. In brief, it is a two-stage longitudinal study of the prevalence and incidence of dementia in a community sample of 2459 persons aged 65 and over. Screening was conducted with the Community Screening Interview for Dementia (CSI-D). Second-stage clinical assessment was conducted on a random sample selected on the basis of screen score performance, but with over sampling for poor performance. Included in the second-stage assessment was a neuropsychological test battery that consisted, among others, the Mini-Mental State Examination (MMSE).

Only those who met the criteria of both the ICD-10 and DSM-IIIR received a diagnosis of dementia.

The data presented here is from a prospective study which was collected during the prevalence phase of the project which took place in 1992-93.

A total of 56 individuals had CT evaluations: 20 (7 males and 13 females), with a diagnosis of dementia formed the study group and 36 (15 males and 21 females) that were considered free of significant cognitive impairment constituted the controls. The mean age of the study group 75.6 (+/-6.8) years while that for the control group was 74.8 (+/-9.6) years. The mean score on the MMSE for the study group was 11.6 (+/-5.0) while that of the control was 22.4 (+/-3.2).

All subjects were free of a history of head trauma, encephalitis, meningitis, epilepsy, multiple sclerosis, cerebral palsy, prolonged drug or alcohol abuse.

Radiological Assessment

All the CT scans were un-enhanced and performed on a G.E 9000 model in a standard fashion with an approximate 15° tilt from the canthomeatal line and done at 5mm thickness in the posterior fossa sand 10mm through the remaining portion of the brain.

The scans were done by the same radiographer and interpreted by two radiologists who were all times blind to the clinical status of the subjects.

The C/T measures were mostly in line with the method and illustrative pictures of Schintzelein et al[11]. All the measures were obtained by direct tracings of the region of interest of the images produced on the console and using the CT computer "Region of Interest" (ROI) facility provided.

The Brain area (BSA), Bi-frontal ratio (BFR), Bi-caudate ratio (BCR) and Pre-pontine ratio (PPR) measurements were taken at the slice level corresponding to the Pineal gland and Foramen of Monro (P/FOM), while that of the Lateral Ventricular Brain ratio (LVBR) was taken from the slice corresponding to the widest region of the body of the cerebral ventricle

Brain Area (BSA):

This is defined as the area of brain, within the inner table of the skull at the P/FOM slice level.

Bifrontal Ratio (BFR):

This is the widest distance from the tips of the anterior horns, divided by the distance between the inner- table of the skull along the same plane.

Bicaudate Ratio (BCR):

This is the point at which the distance between the Caudate nuclei is at its minimum divided by the distance between the inner- table of the skull along the same plane. (Fig 1)

Prepontine Ratio (PPR):

The slice is selected where Pons is most clearly delineated by the fourth ventricle and Prepontine cistern. This is measured along the mid-sagittal line and divided by height of Pons measured along the same line.

Maximum Ventricular Brain Ratio (LVBR):

This is defined as the area of thee body of the Lateral ventricle taken at its widest portion, divided by the Brain slice area at this level of the same slice.

Cortical Atrophy:

Cortical sulci atrophy was assessed with two C-T slices above the level of the lateral ventricles at their widest. Using illustrative pictures obtained from Schintzelein et al[11], four ratings were assigned as follow: 1= No atrophy, 2= Mild atrophy, 3=Moderate atrophy, 4= Severe atrophy (Fig 2)

Data Analysis

All the measures obtained were expressed as Mean (SD), and statistically analysed, using Pearson's correlation, Chi-square and student's t-test with the

level of significance taken at P< 0.05.

RESULTS

The relationship of the clinical diagnosis to the CT measures is shown in Table 1.

Brain Area (BSA): Subjects with dementia had a significantly smaller Mean Brain Area than those without - Fig 3 (142.93+/-91.6 vs. 148.6+/-12.7, P=0.05)

Influence of Age:

Using the BSA as the index, there was a trend for age to be linearly related to brain size in control subjects, with younger control subjects having larger brains than older controls . This trend seems much less applicable among subjects with dementia.

Influence of Sex:

In both the study and the control groups, males had larger BSA than females. However, none of these differences was statistically significant.

Ventricular Measures (VBR):

Table 2 shows all the Ventricular Brain Ratio measurements in the Clinical groups. Even though measures of Bi-caudate ratio (BCR), Bi-frontal ratio (BFR), Maximum Ventricular ratio (LVBR) and Pre-pontine ratio (PPR) suggested that dementia was associated with a lager ventricular sizes. The difference between the Dementia group and the control group reached statistical significance only in respect of the BCR (P=0.04), indicating that BCR is the most reliable indicator of all the Ventricular Brain ratio measures (Fig 4).

Also, while BCR (P=0.04) and BFR (P=0.01) showed positive correlations with age on one hand among controls, no such relationship was observed among subjects with dementia. (Fig 5A & B)

Age did not bear a remarkable relationship with other CT measures in either the subject or the control group.

Influence of Sex:

All the Ventricular measures in the Control group show larger sizes in the Males than the Females, while similar pattern was observed in BCR and PPR in the Dementia group. These differences were not statistically significant

Cortical Atrophy (CA)

In both the study and control, atrophy in both clinical groups ranges from 1-4, with a lower mean (SD) value of 2.38 (0.87) in dementia than the 2.57 (0.7) recorded in the controls. However, this difference was not statistically significant.

Mini-Mental State Examination (MMSE):

As expected, subjects with dementia performed significantly worse on the MMSE than those without dementia (11.6+/-5 vs. 22.4+/-3.2; P=0.00). Among subjects with dementia, lower MMSE was associated with smaller brain size as measured by the BSA (r=0.55; P=0.01), and larger BFR (r=0.18, P=0.05), the LVBR (r=0.20, P=0.05), and the PPR (r=0.2, P=0.05). No such relationships were observed among control subjects.

DISCUSSION:

Dementia of the Alzheimer's type (Alzheimer's disease) is the most prevalent of the degenerative dementias. It is mostly cortical in location with neuro-pathological features of senile plaques, neuro-fibrilary tangles and granuloacuola degeneration, found in the association cortex of the parietal, temporal, frontal lobes and the hyppocampal nuclei[6]. Structural Imaging (C-T and MRI), offers a potential tool in the clinical diagnosis of Alzheimer's disease (AD). AD may be inferred if Cerebral Atrophy can be shown radiologically. Earlier workers[3,8,9,13,15] have reported the neuro-radiological features of cerebral atrophy, which include ventricular dilatation and reduction in brain size.

In this study, we evaluated brain C-T changes in clinically diagnosed Dementia (AD) subjects and non-demented controls. Subjects with dementia had significantly smaller brains than controls. AD patients also had evidence of ventricular dilatation, a finding that is in consonance with those of other workers[9]. In our sample, the BCR was the only ventricular measures that support the impression of a significant dilatation in AD, suggesting that this may be the most sensitive index of cerebral atrophy in this population of dement subjects.

A few cases of significant increase in ventricular volume with age in normal subjects have been reported by other workers[2,5,4] . This pattern was also observed in our study in which the non-demented controls showed a corresponding linear reduction in BSA with age as a result of rise in ventricular volume. However no relationship was found between ventricular volume and age among AD subjects, indicating that the observed radiological changes in this group could not be

attributed solely to ageing but is more likely a result of the pathology of AD.

Among normal subjects, Hartmann et al[14], reported a significantly larger average brain weight in adult males than females. In our study, a larger brain size was observed in males in both the study and the control groups. We also observed a larger ventricular size in males than in females in both groups, an observation similar to those in some previous studies[2,4]. However, none of these observations was statistically significant, thus suggesting that the brain changes reported among subjects with AD can also not be attributed to the effect of gender.

We demonstrated a significant relationship between the levels of cognitive deterioration in AD, as measured by the MMSE, and CT indices of brain atrophy. Such a relationship has been shown by Aylward et al[1] who reported a relationship between deteriorating intellectual functioning in AD and increasing Maximum Ventricular area (LVBR), and Suprasellar cistern ratio (SSCR) respectively.

In conclusion, the significance of our findings revealed that Cortical and Sub-cortical (Central) Atrophy, as evident by large Ventricular sizes, dilated sulci and cisterns, are the persistent Brain morphological changes on CT of Alziemer's in our community, which is similar to those reported in the developed part of the world.

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TABLE 1 : : Relationship of the Clinical Diagnosis to the Mean (SD) of all C/T Measures

C-T Measures	Dementia (AD)N=20 Mean (SD)	Controls N=36 Mean (SD)
Sex (M/F)	7/13	16/20
Age (years)	75.6(6.8)	74.8(9.6)
Brain Area (cm)(BSA)	142.93(91.6)	148.6(12.7)
Bi-caudate Ratio (BCR)	18.5(3)	16.3(4)
Bi-frontal Ratio (BFR)	36.8(5.3)	35.9(7.5)
Maximum ventricle Ratio(LVBR)	7.5(5.4)	6.7(1.7)
Pre-pontine Ratio (PPR)	30.7(10)	29.4(9.9)
Cortical Atrophy	2.3(0.8)	2.6(0.7)
Mini-Mental State Examination (MMSE)	11.6(5)	22.4(3.2)

TABLE 2:Relationship of the Clinical Diagnosis with Ventricular Brain Measures (VBR) and Age in Both Clinical Groups

Age (yrs)	Dementia (mean)				Control (mean)			
	BCR	BFR	LVBR	PPR	BCR	BFR	LVBR	PPR
60-70	18.2	34.1	5.6	30.9	12.5	35.85	6.25	23.5
71-80	18.05	38.9	8.17	34.6	16.4	34.4	6.95	26.1
81-90	17.65	33.9	6.7	24.5	19.75	37.5	8.05	29.75
91-100	23	39.3	11.4	18.4	17	42.8	8.3	29.5

TABLE 3: Relationship of the Clinical Diagnosis with Brain Area (BSA), Ventricular Measures (VBR) and Gender

C/T Measures	Dementia {mean (SD)} N=20		Controls {mean (SD)} N=36	
	Male	Female	Male	Female
Brain Area (BSA) (cm)	146.5(8.9)	140.9(9.1)	159(10.2)	141.2(9)
Bi-caudate Ratio (BCR)	18.9(2.7)	18.2(4)	16.9(2.6)	15.8(2.3)
Bi-frontal Ratio (BFR)	34.2(7.1)	38.3(3.7)	37.8(3.4)	34.5(3.2)
Maximum Ventricular Ratio (LVBR)	7.6(3.2)	7.8(2.5)	7(1.5)	6.9(8.6)
Pre-pontine Ratio (PPR)	32.4(13)	29.7(9.9)	30.8(8.7)	28.4(10.9)

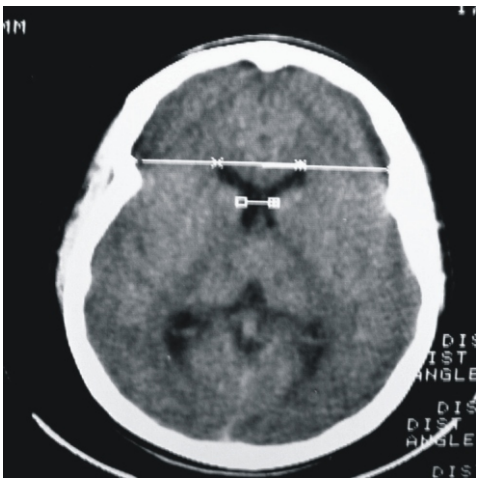
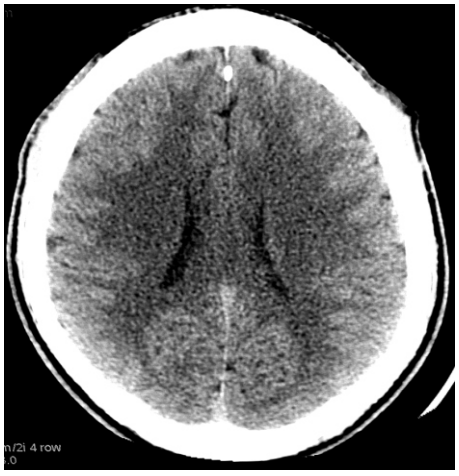
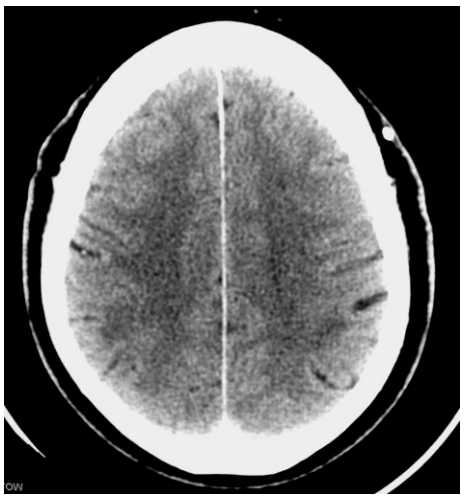


Fig1. Brain CT Images of Bicaudate Ratio measurements at the level of Foramen of Monro
xy = Bicaurdate Diameter
cd = Internal Brain Diameter
xy/cd = Ventricular Ratio

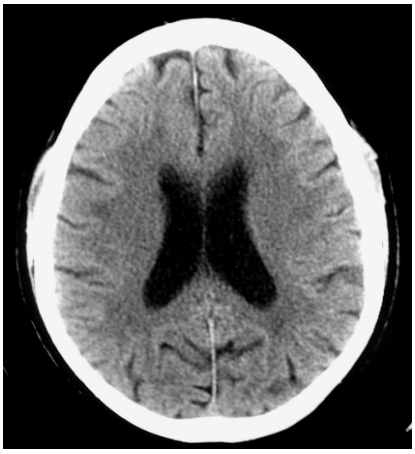
Fig 2: Brain CT images of cortical atrophy gradings at slices above the body of the lateral ventricles in dementia subjects



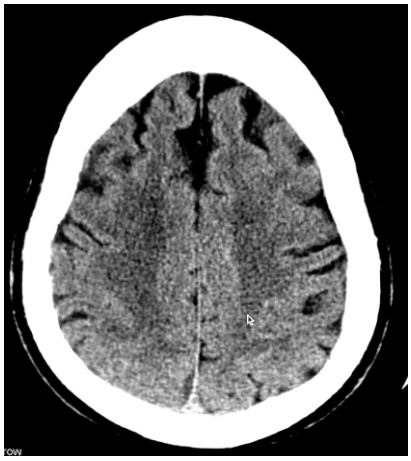
GRADE 1 = N0RMAL



GRADE 2 = MILD



GRADE 3= MODERATE



GRADE 4= SEVERE

FIG 3. Graphical representation of brain area (BSA) showing smaller areas in dementia than control

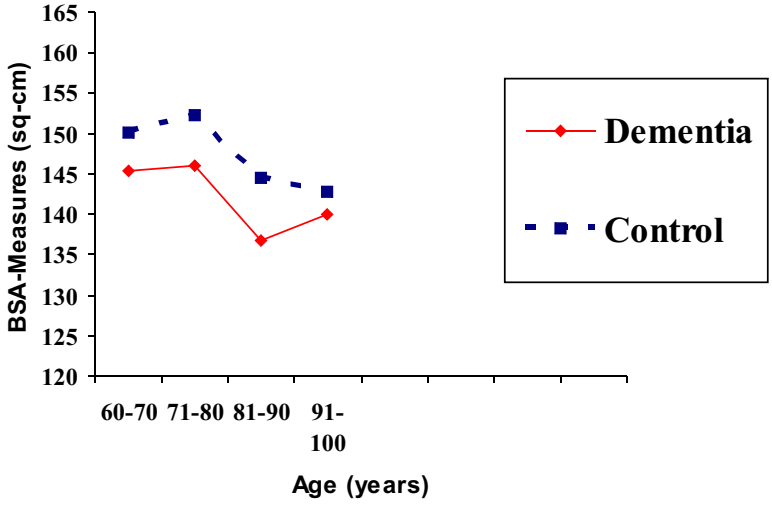


Fig 4: Graphical representation of the BCR in both clinical groups showing larger ventricular sizes in dementia than control

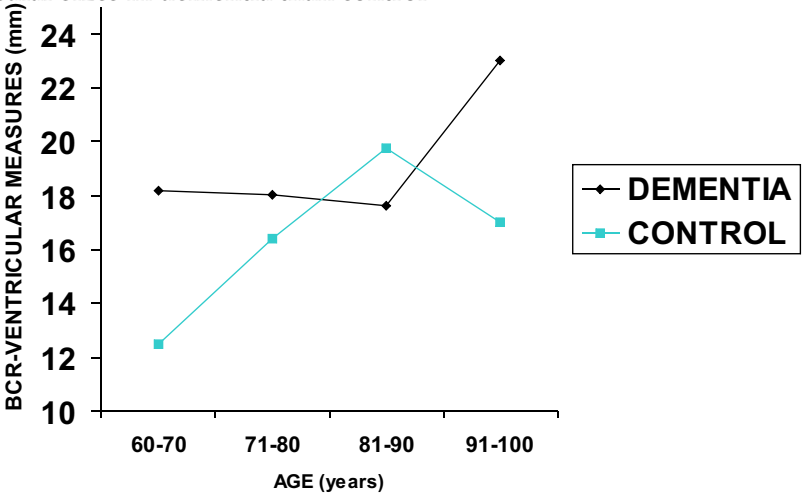


FIG 5A: Graphical representation of the positive correlation of BCR & BFR in the control group

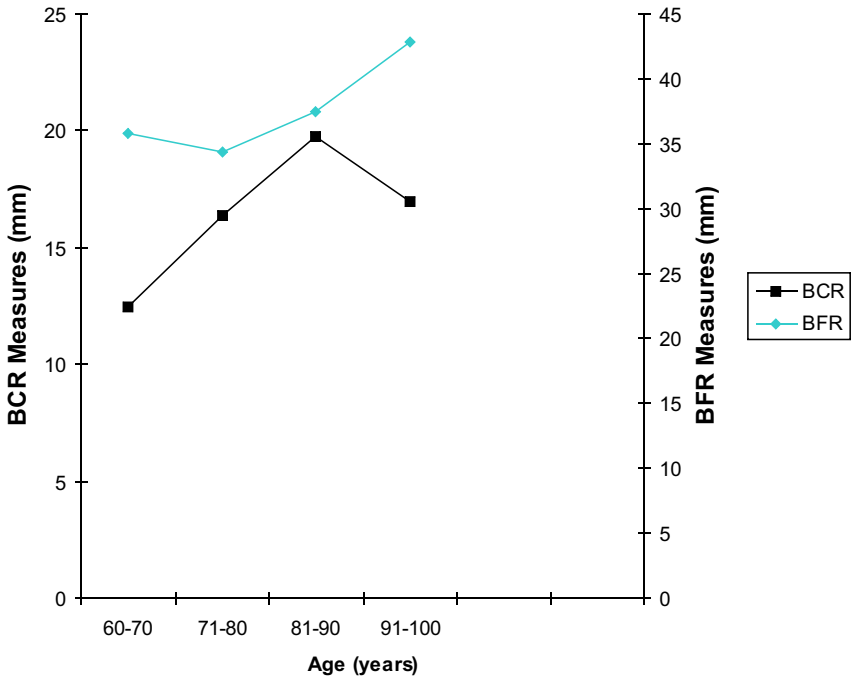
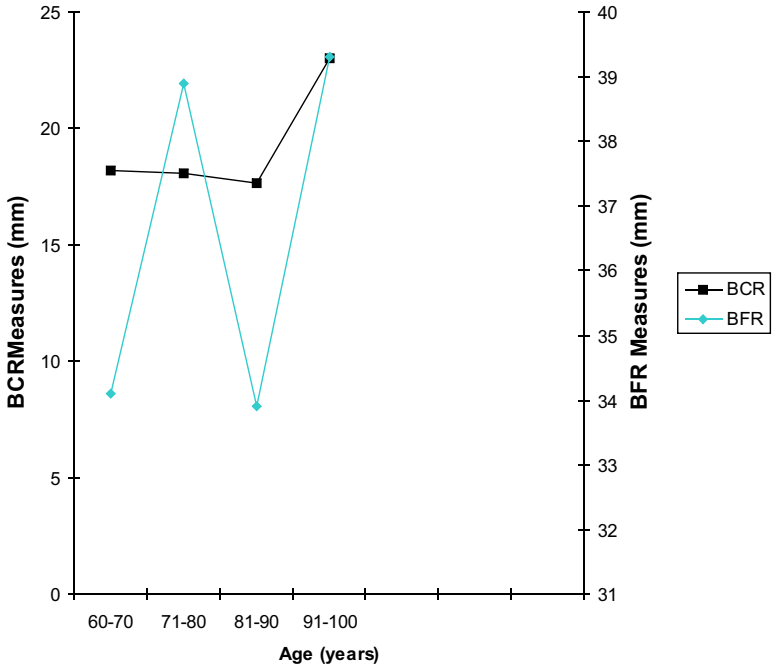


FIG 5B: Graphical representation of the non-correlation of BCR & BFR in dementia



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