Research Article

A Computerised Tomographic assessment of structural changes in the human brain with aging

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Abstract

Background: Computerised Tomography (CT) scan of brain is a useful tool to detect structural changes in the brain with accuracy and safety. Aging is associated with gradual loss of normal brain tissue that can cause greater levels of decline in cognition and leads to low quality of life. This decline is found to occur only after a particular age. Evidence suggests that early life mental ability may help protect against dementia. With aging, the number of nerve cells usually decreases, although the number lost varies from person to person. The brain tends to compensate for these losses by redundancy, by making new synapses between the existing nerve cells and in some cases by producing new nerve cells especially after brain injury or a stroke. The sub-ventricular zone retains some neural stem cells which are capable of forming new nerve cells and synapses forming the basis for plasticity. With improvements in health care systems, the life expectancy has gone up; as a result, the number of elderly in the population has increased even in developing countries like India. Hence, importance is given to strategies to preserve cognitive and physiologic functions and prevent age related diseases. The gray and white matters are lost in normal aging process leading to dementia though variations between individuals do exist. The volume or size of the ventricular system of the brain is considered to be one of the general parameters of brain development. CT is a safe and non-invasive method to assess the ventricular system of the brain. It is a painless, sophisticated x-ray procedure that obtains images of parts of the body that cannot be seen. Therefore these scans often result in earlier diagnosis and more successful treatment of many diseases. Though computerized tomography imaging does involve x-rays, the diagnostic benefits generally outweigh the risks of radiation exposure. The nuclei and white matter that abut the cerebral ventricles define their volume and size and the ventricles of the brain and cortical sulci. The enlargement is not uniform throughout the ventricular system and is found to be relatively early and significantly more in the frontal brain regions which have a more complex structure with late maturation.

Keywords: CT scan, Aging brain, Cerebral ventricles, Cortical sulci

1. Introduction

Aging is a normal physiological process with some degree of decline in cognitive functions like memory and reasoning and those with greater levels of decline in cognition are more likely to have low quality of life. Brain function remains relatively stable during most of adulthood and may decline after a certain age. Evidence suggests that early life mental ability may help protect against dementia. With aging, the number of nerve cells usually decreases, although the number lost varies from person to person. The brain tends to compensate for these losses by redundancy, by making new synapses between the existing nerve cells and in some cases by producing new nerve cells especially after brain injury or a stroke. The sub-ventricular zone retains some neural stem cells which are capable of forming new nerve cells and synapses forming the basis for plasticity. With improvements in health care systems, the life expectancy has gone up; as a result, the number of elderly in the population has increased even in developing countries like India. Hence, importance is given to strategies to preserve cognitive and physiologic functions and prevent age related diseases. The gray and white matters are lost in normal aging process leading to dementia though variations between individuals do exist. The volume or size of the ventricular system of the brain is considered to be one of the general parameters of brain development. CT is a safe and non-invasive method to assess the ventricular system of the brain. It is a painless, sophisticated x-ray procedure that obtains images of parts of the body that cannot be seen. Therefore these scans often result in earlier diagnosis and more successful treatment of many diseases. Though computerized tomography imaging does involve x-rays, the diagnostic benefits generally outweigh the risks of radiation exposure. The nuclei and white matter that abut the cerebral ventricles define their volume and size and the ventricles of the brain and cortical sulci. The enlargement is not uniform throughout the ventricular system and is found to be relatively early and significantly more in the frontal brain regions which have a more complex structure with late maturation.

The aim of the present study was to assess the size of the ventricular system with normal aging process using CT scan.

2. Material and Methods

98 healthy subjects of both sexes between the ages of 20-85 years were included in the study. Patients attending the Radiology and Imageology unit of a medical college hospital who had come for a CT scan of brain were included in the study. The subjects were divided into 6 groups. Subjects with Diabetes mellitus, hypertension, mental deficits, family history of any neurological illness and any emotional or psychological trauma were excluded from the study. Computerized Tomography scan using Toshiba Sub Second Real time Helical CT Scanner, Model – Astone and Printer – DRYSTAR 3000 AGFA were used to study the structural changes in brain due to aging.

A semi - quantitative estimation of cerebral atrophy with the use of indices, which take into account the widths of cerebral ventricles and subarachnoid spaces was done. In the study participants6; the parameters studied were Anterior Horn Quotient which is the ratio between the distance between the two occipital horns of lateral ventricle and the maximum distance between the two frontal horns of lateral ventricle and is denoted as F/C and it should normally be ≥ 3.7. The Hekmann Index denoted by C+D is the sum of maximum distance (C) and minimum distance (D) between the two frontal horns of lateral ventricles and should normally be ≤ 5cm. The width of the third ventricle (E) should be ≤ 7mm and Pars centralis index (A/B) which is the ratio between the width of the intracraniel space and width of the body of lateral ventricle should be ≥ 4.1. Frontal interhemispheric fissure should be ≤ 4mm and width of cortical sulci should be ≤ 3mm. Informed consent was taken from all the subjects participating in the study and the Institute Ethics committee permission was obtained.
Analysed and tabulated using Epi info 2000 software. Computerised Tomography scan results showing width of CSF spaces.

### Table 1: Anterior Horn Quotient (F/C)

| S.No. | Age Groups    | N  | Mean Age (yrs) | SD (±) | Mean F/C | SD (±) |
|-------|---------------|----|----------------|--------|----------|--------|
| 1     | Group I - 21-30yrs | 11 | 25             | 3.63   | 2.01     | 0.48   |
| 2     | Group II - 31-40yrs | 19 | 37.58          | 2.71   | 1.99     | 0.41   |
| 3     | Group III - 41-50yrs | 18 | 45.83          | 3.11   | 1.19     | 0.47   |
| 4     | Group IV - 51-60yrs | 18 | 56.78          | 3.02   | 1.86     | 0.28   |
| 5     | Group V - 61-70yrs | 20 | 68.65          | 2.13   | 1.78     | 0.39   |
| 6     | Group VI - 71+ yrs | 12 | 78.58          | 2.62   | 1.72     | 0.25   |

The normal value for anterior horn quotient (F/C) ≥ 3.7. From group I to group VI, the F/C was less than 3.7. Chi square = 0.45 and p = 0.5 which is not significant.

### Table 2: Huckmann Index (C+D)

| S.No. | Age Groups    | N  | Mean Age (yrs) | SD (±) | Mean C+D (cm) | SD (±) |
|-------|---------------|----|----------------|--------|---------------|--------|
| 1     | Group I - 21-30yrs | 11 | 25             | 3.63   | 4.13         | 0.83   |
| 2     | Group II - 31-40yrs | 19 | 37.58          | 2.71   | 4.15         | 0.79   |
| 3     | Group III - 41-50yrs | 18 | 45.83          | 3.11   | 4.87         | 0.65   |
| 4     | Group IV - 51-60yrs | 18 | 56.78          | 3.02   | 4.82         | 0.99   |
| 5     | Group V - 61-70yrs | 20 | 68.65          | 2.13   | 5.03         | 1.03   |
| 6     | Group VI - 71+ yrs | 12 | 78.58          | 4.62   | 5.35         | 0.67   |

Normal value for Huckmann Index (C+D) ≤ 5cm. Group V and group VI had more than 5 cm. Chi square = 0.56 and p = 0.45 which is not significant.

### Table 3: Width of third ventricle (E)

| S.No. | Age Groups    | N  | Mean Age (yrs) | SD (±) | Mean E (mm) | SD (±) |
|-------|---------------|----|----------------|--------|-------------|--------|
| 1     | Group I - 21-30yrs | 11 | 25             | 3.63   | 3.81        | 1.6    |
| 2     | Group II - 31-40yrs | 19 | 37.58          | 2.71   | 4.47        | 1.05   |
| 3     | Group III - 41-50yrs | 18 | 45.83          | 3.11   | 4.94        | 1.92   |
| 4     | Group IV - 51-60yrs | 18 | 56.78          | 3.02   | 6.55        | 2.38   |
| 5     | Group V - 61-70yrs | 20 | 68.65          | 2.13   | 6.5         | 2.16   |
| 6     | Group VI - 71+ yrs | 12 | 78.58          | 4.62   | 7.66        | 2.57   |

The normal value for the width of third ventricle (E) is ≤ 7mm. In groups from I to V, the size of the third ventricle was less than 7mm, whereas only in group VI E was found to be more than 7 mm. Chi- square = 0.35 and p = 0.55 which is not significant.

### Table 4: Pars Centrals Index (A/B)

| S.No. | Age Groups    | N  | Mean Age (yrs) | SD (±) | Mean A/B         | SD (±) |
|-------|---------------|----|----------------|--------|-----------------|--------|
| 1     | Group I - 21-30yrs | 11 | 25             | 3.63   | 5.88            | 1.84   |
| 2     | Group II - 31-40yrs | 19 | 37.58          | 2.71   | 5.25            | 0.77   |
| 3     | Group III - 41-50yrs | 18 | 45.83          | 3.11   | 5.13            | 1.2    |
| 4     | Group IV - 51-60yrs | 18 | 56.78          | 3.02   | 5.05            | 1.37   |
| 5     | Group V - 61-70yrs | 20 | 68.65          | 2.13   | 4.98            | 0.65   |
| 6     | Group VI - 71+ yrs | 12 | 78.58          | 4.62   | 4.77            | 2.61   |

The normal value for pars centralis index (A/B) is ≥ 4.1. Pars centralis index is the space at the junction of the body of lateral ventricle with posterior and inferior horns. All groups from I to VI had this value above 4.1. Chi- square was 0.12 and p = 0.73 which is not significant.

### Table 5: Width of Frontal Interhemispheric fissure (FIF)

| S.No. | Age Groups    | N  | Mean Age (yrs) | SD (±) | Mean FIF (mm) | SD (±) |
|-------|---------------|----|----------------|--------|---------------|--------|
| 1     | Group I - 21-30yrs | 11 | 25             | 3.63   | 3.5           | 1.25   |
| 2     | Group II - 31-40yrs | 19 | 37.58          | 2.71   | 3.68          | 1.38   |
| 3     | Group III - 41-50yrs | 18 | 45.83          | 3.11   | 3.72          | 1.32   |
| 4     | Group IV - 51-60yrs | 18 | 56.78          | 3.02   | 3.7           | 0.92   |
| 5     | Group V - 61-70yrs | 20 | 68.65          | 2.13   | 4             | 1.26   |
| 6     | Group VI - 71+ yrs | 12 | 78.58          | 4.62   | 4.58          | 1.38   |

The normal value for frontal interhemispheric fissure (FIF) is ≤ 3mm. In all groups from I to VI, the width of FIF was more than 3 mm. Chi-square = 0.05 and p= 0.82 which is not significant.

### Table 6: Width of Cortical Sulci (S)

| S.No. | Age Groups    | N  | Mean Age (yrs) | SD (±) | Mean S (mm) | SD (±) |
|-------|---------------|----|----------------|--------|-------------|--------|
| 1     | Group I - 21-30yrs | 11 | 25             | 3.63   | 3.5         | 1.25   |
| 2     | Group II - 31-40yrs | 19 | 37.58          | 2.71   | 3.68        | 1.38   |
| 3     | Group III - 41-50yrs | 18 | 45.83          | 3.11   | 3.72        | 1.32   |
| 4     | Group IV - 51-60yrs | 18 | 56.78          | 3.02   | 3.7         | 0.92   |
| 5     | Group V - 61-70yrs | 20 | 68.65          | 2.13   | 4           | 1.26   |
| 6     | Group VI - 71+ yrs | 12 | 78.58          | 4.62   | 4.58        | 1.38   |

The normal value for the width of cortical sulci (S) is ≤ 3mm. The cortical sulcal width in all groups was found to be more than 3mm. Chi- square was 11.83 and p = 0.0008 (<0.05) which was found to be highly significant.

### 4. Discussion

Age is an independent factor contributing to loss of cerebral tissue. Aging leads to gross and histopathological changes in the brain. Brain shrinks and ventricles expand with healthy aging. Different areas of the brain react differently to aging. The pattern of change is highly heterogeneous as per some studies and largest changes are seen in the neocortical regions like prefrontal and temporal cortices. These variations may be explained by...
genetic factors as the development and morphogenesis of neocortical regions are autonomous processes that are controlled by multiple independent genes\textsuperscript{13}. Rather than loss of neurons, shrinkage of neurons, shrinkage of synaptic spines and low number of synapses account for loss of brain tissue along with greatly reduced length of myelinated axons. With regression of brain tissue especially the median nuclei of the thalami, there is ballooning of the 3rd ventricle and rounding of the angles of the lateral ventricles.

Table 1 show the coefficient of frontal horns, which is given by the ratio between the width of occipital horns and width of frontal horns of lateral brain ventricles. This ratio is found to decrease gradually from 2\textsuperscript{nd} to 7\textsuperscript{th} decade of life though the decrease is not found to be significant indicating that tissue loss occurs gradually till very late in life.

The Huckmann index, as shown in table 2 is the sum of the width of the frontal horns of lateral brain ventricles and width of interpolar regions, also gives an estimation of cerebral atrophy. In the present study, there is only a small increase in this index with age and is not found to be significant. It is only after the age of 60 years (group V and VI) the Huckmann’s index has crossed the normal values. This maybe because of the fact that atrophic changes take place very late in life almost in the 7\textsuperscript{th} or 8\textsuperscript{th} decade of life in the lateral cortex causing minimal brain tissue loss. This may also be the reason for very late changes taking place in the 3\textsuperscript{rd} ventricular size which is found to increase only in the 7\textsuperscript{th} decade of life as shown in table 3.

The pons centrals index gives the ratio of width of skull to width of lateral parts of both lateral ventricles and is not found to be significant. Width of frontal interhemispheric fissure also shows some increase from younger ages and more in the 7\textsuperscript{th} decade of life. This is in accordance with previous studies which attribute this change in neocortical regions to their complex structure and late maturation.

There is also widening of cortical sulci in the present study as shown in table 6 where the widening is found to start early in life, as early as the 3\textsuperscript{rd} decade leading to lesser curvature and depth as also observed in previous studies\textsuperscript{17}. This change in geometry of cortical folding with aging can lead to cognitive decline and is probably due to loss of grey matter which leads to thinning and widening of the cortical sulci, also causing a secondary widening of the ventricles of the brain\textsuperscript{15,16}.

**Recommendations & Conclusion**

Computerised Tomography scan is a non-invasive and safe method to assess the changes taking place in brain with the normal physiological aging process. If adopted by geriatric departments as a routine screening tool, several disorders of the brain if any, can be detected at an early stage and necessary intervention may be done to avoid progress of the disease to a critical level. Also, the onset of severity of age related changes in the brain can be delayed by adopting lifestyle changes like being mentally and physically active with advancing age.

**References**

1. Salthouse T. Major Issues in Cognitive Aging. Oxford University Press, USA, 2010.
2. McGurn B, Deary II, Starr JM. Childhood cognitive ability and risk of late-onset Alzheimer and vascular dementia. *Neurology* 2008; 71: 1051–6.
3. Ikram MA, Vrooman HA, Vemouq MW et al. Brain tissue volumes in relation to cognitive function and risk of dementia. *Neurobiol Aging* 2010; 31:378–86.
4. Gilmore JH, van Tol J, Kliwer MA, et al. Mild ventriculomegaly detected in utero with ultrasound: clinical associations and implications for schizophrenia. *Schizophr Res* 1998; 33:133-40.
5. Raz N, Rodrigue KM, Head D, Kennedy KM, Acker JD. Differential aging of the medial temporal lobe: a study of a five-year change. *Neurology* 2004a; 62:433-439.
6. Sebastian Lange et al; Cerebral spiral computerized tomography, chapter- Degenerative diseases, cerebral atrophy; 104 – 105.
7. Sanne M. Manschot, Augustina M.A. Brands, Jeroen van der Grond, Roy P.C. Kessels, Ale Algra et al; Brain Magnetic Resonance Imaging Correlates of Impaired Cognition in Patients with Type 2 Diabetes. *Diabetes* 2006, April; 55(4), 1106-1113.
8. York GK, Steinberg DA. Huhlincs Jackson’s theory of recovery. *Neurology* 1995; 45:834-38.
9. Fjell AM, Walhovd KB. Structural brain changes in aging: courses, causes and cognitive consequences. *Rev Neurosci.* 2010; 21(3):187-221.
10. Allen JS, Bruss J, Brown CK, et al; Normal neuroanatomical variation due to age: the major lobes and a parcellation of the temporal region. *Neurobiol Aging* 2005; 26:1245-60.
11. Kennedy KM, Erickson KI, Rodrigue KM et al; Age related differences in regional brain volumes: a comparison of optimized voxel – based morphometry to manual volumetry, *Neurobiol Aging* 2009; 30:1657-76.
12. Klopouzos G, Chetelat G, Baron JC et al. Voxel – based mapping of brain gray matter volume and glucose metabolism profiles in normal aging. *Neurobiol Aging* 2009; 30:112-24.
13. Piao X, Hill RS, Bodell A, Chang BS, Basel-Vanagaitë L, Straussberg R et al; G protein-coupled receptor-dependent development of human frontal cortex. *Science* 2004; 303:2033–2036.
14. Im K, Lee JM, Seo SW, Hyung Kim S, Kim SI, et al. Sulcal morphology changes and their relationship with cortical thickness and gyral white matter volume in mild cognitive impairment and Alzheimer’s disease. *Neuroimage* 2008; 43: 103–113.
15. Kochunov P, Mangin JF, Coyle T, Lancaster J, Thompson P, et al. Age-related morphology trends of cortical sulci. *Hum Brain Mapp* 2005; 26: 210–220.
16. Liu T, Wen W, Zhu W, Trollor J, Reppermund S, et al. The effects of age and sex on cortical sulci in the elderly. *Neuroimage* 2010; 51: 19–27.