Original Article

Age and Gender Differences in Morphometric Measurements of Brain Stem Using Magnetic Resonance Imaging in Healthy Indian Adults

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Abstract

Background: Morphometric changes in the brain stem can be an early indicator for ongoing physiological or pathological changes. Establishing age- and gender-matched linear morphometric values of the brain stem serves as a useful reference for comparison. **Aims and Objectives:** This study aimed to determine normal measurements of brain stem structures in healthy Indian adults and to establish age and gender differences in brain stem measurements if any. **Materials and Methods:** This hospital-based cross-sectional study was conducted from November 2020 to January 2021 on patients referred to the department of radiodiagnosis for magnetic resonance imaging (MRI) of the brain. Baseline data and linear midsagittal measurements on MRI were recorded. **Results:** A total of 142 patients were included in the study. The average measurements for midbrain, pons, medulla at pontomedullary (PM), and medulla at cervicomedullary junction are 1.67 ± 0.17 cm (mean ± standard deviation [SD]), 2.16 ± 0.18 cm (mean ± SD), 1.39 ± 0.16 cm (mean ± SD), and 1.08 ± 0.13 cm (mean ± SD), respectively. Significant reduction in brain stem measurements at all levels with $P < 0.05$ were recorded with increase in age except for the medulla at the PM junction which remained constant. There was no significant difference in brain stem measurements between males and females. **Conclusion:** Normal reference value for AP diameter of the brain stem in healthy Indian adults showed statistically significant reduction at various levels with advancing age. There were no statistically significant gender differences in sagittal diameter of the midbrain, pons, and medulla.

Keywords: Age and gender differences, brain stem morphometry, magnetic resonance imaging

Introduction

The brain stem, a critical midline functioning unit consists of the midbrain, pons, and medulla. It plays a pivotal role in the integration of various motor, sensory, sympathetic, and parasympathetic activities.[1] Normal process of aging in adults is known to be associated with volume reduction of the posterior fossa neurostructures. Similarly, there are various pathological processes including neurologic disorders such as Parkinson's disease, Alzheimer's disease, spinocerebellar ataxia, and schizophrenia that alter its morphology and dimensions.[1,2] Magnetic resonance imaging (MRI) has well-established role in the assessment of human neuroanatomy. Some diffusely infiltrating tumors may be detected by changes in the size of the midbrain rather than demonstrating differences in signals due to changes in relaxation times on MRI.[3]

Aging can negatively influence various brain stem-mediated activities such as sympathetic outflow, vestibulo-ocular reflexes, and cardiovascular reflexes. Gender differences have been noticed in morphometry of the posterior fossa structures. Various studies indicate that these changes seen in the brain stem with aging and in different genders could be precursors for subclinical neurodegenerative conditions.[4]

Sex differences in cerebral and brain stem shrinkage with aging could result from various factors such as hormonal variations and hypertension. Interactions with environmental factors, such as exposure to toxins and trauma can also lead to loss of

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brain tissue.[5] Thus, the awareness of normal neuroanatomic variability with respect to the age and gender of an individual is important for understanding various physiological and pathological changes.[4]

Imaging techniques such as computed tomography (CT) and MRI provide an objective assessment of intracranial structures.[1] MRI is considered superior to CT in providing reliable and accurate neuroanatomical details about brain stem in relation to normal aging, gender or its involvement in neurological diseases.[6]

The anatomical structures in the brain can be measured quantitatively in terms of linear measurements, which can be performed more quickly and do not require additional software.[7,8] Thus, MRI can be used as a simple and rapid means of determining brain stem measurements.[9]

There are various studies quoting the changes in the supratentorial structures with increasing age and in different genders of a population. Very few studies are available recording the changes in infratentorial structures.[2]

Cumulative research studies on brain stem morphometry in the healthy Indian adult population are quite few. There is a need for a reference normative data based on age and gender differences in our population. The purpose of this study is to arrive at a normative data for simple linear morphometric measurements of brain stem on MRI.

Materials and Methods

Source of data

This was a cross-sectional study conducted from November 2020 to January 2021 on those who were referred to the department of radio-diagnosis for MRI of the brain and met the inclusion and exclusion criteria. The study was approved by the institutional ethics committee. Informed consent was taken from the patients regarding their willingness to participate in the study.

Study design

This was a hospital-based cross-sectional study.

Sample size

The sample size was calculated using the formula mentioned below from a study by *S. Ö.* Polat *et al*.[1]

Where,

The size of effect that is clinically worthwhile to detect, $(d) = 0.62$.

The probability of falsely rejecting a true null hypothesis $(\alpha) = 0.05$, $Z_\alpha = 1.96$.

The probability of failing to reject a false null hypothesis $(\beta) = 0.80$, $Z_\beta = 1.282$.

The standard deviation of the population being studied (SD) = 2.20.

Considering an α error of 5% the required sample size will be 112.

Inclusion criteria

- All patients were referred for an MRI of the brain with no brain stem abnormality.

Exclusion criteria

- Patients of age <18 years
- Patients with any brain stem abnormality on imaging
- Those with a history of psychiatric illness and neurological disorders such as Alzheimer's, dementia, multiple sclerosis, and Parkinson's disease
- Prior neurosurgical intervention.

Method of collection of data

Informed consent was taken. Baseline information of the patients participating in the study was recorded. MRI of the brain was performed on patients fulfilling the inclusion/exclusion criterion on 1.5 Tesla, 18 channel, MRI Scanner (Siemens® MAGNETOM Avanto®).

Brain stem morphometry

Linear measurements were taken on T1 sagittal image in (cm) as follows

- Midbrain: The anteroposterior (AP) diameter between superior and inferior colliculi
- Pons: The AP diameter between the anterior surface of the pons to the floor of the fourth ventricle
- Medulla Oblongata: The AP diameter perpendicular to the longitudinal axis was measured at two levels:
  a. At the pontomedullary (PM) junction
  b. Just above the posterior kink at the cervicomedullary (CM) junction.

Statistical analysis

Data were entered into a Microsoft Excel sheet. The measurable variables were analyzed. The *t*-test and ANOVA tests were used for the comparison of the mean values.

The statistical procedures were performed with the help of an SPSS statistical package (version 26) and OPenEpi version 3.01 (Chicago, Illinois, USA). $P < 0.05$ ($P < 0.05$) was considered statistically significant.

Results

A total number of 142 participants were included in this study, out of which 82 (57.7%) were males and 60 (42.3%) were females as shown in Figure 1 with a mean age of 40.59 ± 14.66 years (mean ± SD).

Gender distribution

Age group distribution

Participants were classified into five different age groups, from above 18 years of age as represented in Figures 2 and 3. The mean age of 40.59 ± 14.66 years (mean ± SD) was recorded.

Brain stem measurements

The overall mean AP diameters of brain stem measured at various levels are shown in Table 1. The mean AP diameter at the level of the midbrain is ~1.67 ± 0.17, pons is ~2.16 ± 0.18, medulla at PM junction is 1.39 ± 0.16, and medulla at CM junction is ~1.08 ± 0.13, respectively.

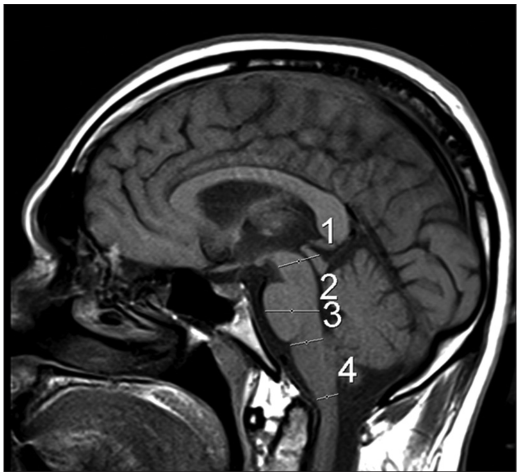

Figure 1: MRI of the brainT1-weighted sagittal image demonstrating midsagittal anteroposterior diameters of the midbrain (1), pons (2), medulla at the pontomedullary junction (3), and medulla at cervicomedullary junction, (4), respectively. MRI: Magnetic resonance imaging

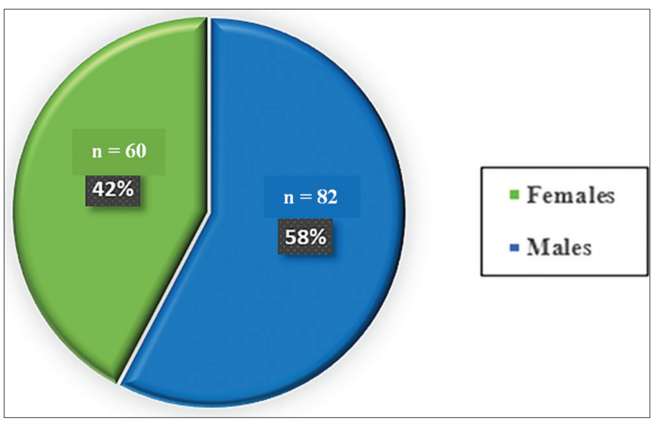

Figure 2: Gender distribution

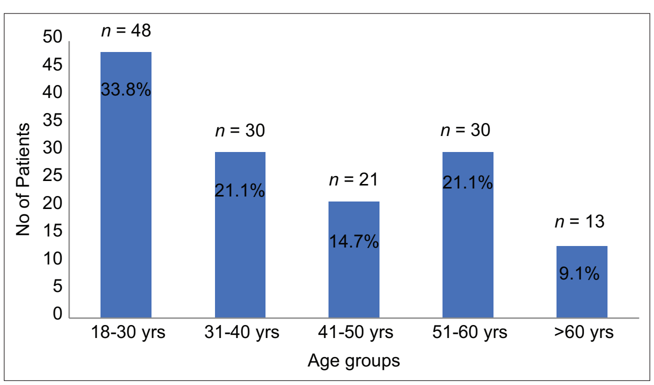

Figure 3: Age group distribution

Brainstem measurements classified according to age groups

The mean AP diameters of respective age groups were calculated and compared for statistical significance.

With increasing age, reduction in brain stem measurement for midbrain, pons, and medulla oblongata at *P* values as shown in Table 2. The maximum diameter for the midbrain was observed at 18–30 years of age, following which gradual decline of up to ~11 mm was noted by the age of >60 years. Similarly, the maximum diameter of pons was observed at the age group of 41–50 years (2.23 ± 0.18) following which a reduction of ~13 mm was noted by the sixth decade of life. The maximum diameter of the medulla was observed in the third to fourth decade at both PM and CM levels with a drop of ~7 mm at the CM junction by the age of 60 years. However, the changes in the diameters at the PM junction are not statistically significant ($P = 0.69$).

Gender differences in brain stem diameters

Table 3 shows that the mean AP diameters of the brainstem at various levels are insignificant ($P > 0.05$) with respect to the gender of patient.

Discussion

The brain stem is the relay center of the human brain which connects the cerebrum and spinal cord. It comprises the midbrain, pons, and medulla oblongata which control a number of important vital functions of the body, apart from housing various cranial nerve nuclei within. Thus, any pathology concerning these areas would reflect on the brain stem morphology and dimensions. Our study aims to obtain an age- and gender-matched normative reference data for various parts of the brain stem that can be extrapolated for physiologic/pathological change.

In our study, we evaluated the linear midsagittal measurement of parts of the brain stem in 142 patients referred for MRI. The overall mean diameters of brain stem among both males and females were found to be 1.67 ± 0.17 cm (mean ± SD) at midbrain, 2.16 ± 0.18 cm (mean ± SD) at pons, 1.39 ± 0.16 cm (mean ± SD) and 1.08 ± 0.13 cm (mean ± SD) for medulla oblongata at the PM and CM junction, respectively. This was similar to results obtained by Sing *et al*.,[3] who recorded the mean diameters of 1.7 ± 0.12 cm (mean ± SD) at midbrain, 2.27 ± 0.13 cm (mean ± SD) at pons, and

Table 1: Morphometric measurements of brain stem structures

Brain stem diameters	Minimum (cm)	Maximum (cm)	Mean±SD
Midbrain	1.12	2.20	1.67±0.17
Pons	1.70	2.60	2.16±0.18
Medulla at PM junction	1.13	1.51	1.39±0.16
Medulla at CM junction	0.74	1.81	1.08±0.13

SD: Standard deviation, PM: Pontomedullary, CM: Cervicomedullary

Table 2: Distribution of brain stem diameters (cm) according to age groups of healthy adults

Brain stem structures	Mean±SD					*P*
	Group 1 (18-30 years)	Group 2 (31-40 years)	Group 3 (41-50 years)	Group 4 (51-60 years)	Group 5 (>60 years)	
Midbrain	1.73±0.16 (1.32-2.14)	1.69±0.16 (1.35-2.25)	1.60±0.16 (1.30-2.15)	1.61±0.20 (1.12-2.00)	1.62±0.14 (1.32-1.92)	0.001*
Pons	2.19±0.16 (1.72-2.49)	2.17±0.18 (1.85-2.60)	2.23±0.18 (1.78-2.45)	2.11±0.18 (1.74-2.40)	2.10±0.17 (1.76-2.42)	0.043*
Medulla at PM junction	1.34±0.15 (1.90-2.45)	1.35±0.17 (1.86-2.51)	1.36±0.15 (1.90-2.60)	1.32±0.17 (1.91-2.55)	1.30±0.16 (1.80-2.68)	0.69
Medulla at CM junction	1.07±0.20 (0.78-1.36)	1.10±0.21 (0.81-1.81)	1.01±0.13 (1.82-1.36)	0.98±0.13 (1.74-1.29)	1.0±0.12 (0.82-1.28)	0.012*

*P <0.05; statistically significant. SD: Standard deviation, PM: Pontomedullary, CM: Cervicomedullary

Table 3: Gender differences in brain stem diameters

Parts of brain stem	Males	Females	Mean±SD	*P* (<0.05; significant)
Midbrain	1.68±0.17	1.64±0.18	1.67±0.17	0.62
Pons	2.17±0.18	2.12±0.17	2.16±0.18	0.62
Medulla at PM junction	1.35±0.16	1.34±0.14	1.39±0.16	0.40
Medulla at CM junction	1.09±0.12	1.06±0.15	1.08±0.13	0.06

SD: Standard deviation, PM: Pontomedullary, CM: Cervicomedullary

1.30 ± 0.08 cm (mean ± SD) at medulla oblongata, respectively.

In comparing the brain stem diameters among the five groups as shown in Table 3, the following observations were made: There was a significant decline in the AP diameter of midbrain between the second to sixth decade of life. This is supported by various studies were done by Raininko *et al*.,[9] Elhussein *et al*.[4] and Shah *et al*.[10] who attributed it to age-related decline in nigra neurons and neuronal death or degeneration with nuclei and/or tracts of the midbrain.[4,10] In our study, AP diameters of pons and medulla at CM junction showed significant reduction. The AP diameter of the medullar at the PM junction showed no significant change with advancing age. This was consistent with the study by Raininko *et al*.[9] and Elhussein *et al*.[4] who observed a minimal reduction in the AP diameters of midbrain and pons after 50 years of age.

There was no statistically significant difference in the AP diameters of the midbrain, pons, and medulla oblongata between males and females (P > 0.05). This was in concordance with studies by Elameen and Abd[11] and Polat *et al*.,[1] who stated that there was no relationship between gender and brain stem.

The limitation of our study is that volumetric analysis of brain stem structures was not done which could provide a better understanding and information on brain stem morphometry. We recommend further research on this subject with volumetric analysis.

Conclusion

Thus, MRI can be used as a noninvasive and rapid method of obtaining simple linear measurements of the brain stem. The normal reference value for AP diameter showed a statistically significant reduction in diameters of brain stem structures with advancing age; however, there was no gender association. The normal range given in this study can be acknowledged for the assessment of physiological/pathological change in the brain stem.

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Conflicts of interest

There are no conflicts of interest.

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