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Norms for Brain Stem: A morphometric MRI Based Study

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Abstract: *Many neuroanatomical studies of normal brain character have been reported. The brain stem is the most important anatomical structure in the posterior fossa .Investigations of aging effects on the brain stem is important, in order to understand normal aging process. Sex differences in brain stem neuroanatomy have been observed in several studies.In the current study, the objectives were to study the sex differences and the age-related morphological changes of the brain stem on mid-sagittal MRIs. According to radiologists' reports, mid-sagittal MRIs of 275 normal individuals were evaluated in this study. Mean age: 36.33±23.75 years old (max=91.00years, min=1.00 year).There were 126 males and 149 females. By measuring the brain stem, (mid brain, pons and medulla oblongata) results were saved in the computer. Calculation of all regions was performed in the screen monitor of MRI machine and the collected data were statistically analyzed by using SPSS software programme version 16. Students's t-test was applied for gender comparisons. To determine the associations between age and measurements, person correlation coefficients were calculated. Norms for brain stem were established. No significant gender difference was recorded in the brain stem favoring midbrain (p<0.088) ,pons (p<0.940) and medulla oblongata(p<0.485). A-significant age-associated reduction in brain stem compartments was found at p<0.000 for mid brain, pons and medulla oblongata diameters. The normal ranges given in this study can be used for assessment of changes in cases that believed to have neurodegenerative disorders.*

Keywords: *brain stem, magnetic resonance, neuroscience*.

I. Introduction

An awareness of normal neuroanatomic variability is important for understanding pathologic changes. In regard to the posterior fossa structures, the cumulative research studies are quite few and there is a need for normative data. Aging is ubiquitous to the individual circumstance. [1] Previous studies were obtained regarding the brain neuroanatomic studies and ages effect [2], using advanced imaging technology [3].Studies have established that the normal aging is associated with morphological changes in the brain, and posterior fossa neurostructure .[4,5,6]Despite these effects, reported brainstem related changes remains parse due to technical limitations of imaging, segmenting, and statistically analyzing data from this region. [7, 8,9] Aging is known to negatively impact on several brainstem-mediated functions, [10] sympathetic outflow [11] vestibular-ocular reflexes [12] and cardio vascular reflexes. [13] Post-mortem reports indicate that changes within the brainstem sub-nucleido take place during aging [11] some of which may be early precursors for subclinical neuro degenerative disease. [14]

Imaging modalities were used to characterize the brain anatomy. Methods for measuring the pons on CT, and that of the mesencephalon on MRI have been described, and normal values for adults were recorded. [15, 16]Volumetric studies are too time-consuming for routine work; volume and area measurements are not possible using the software of some MR imagers; linear measurements can be made rapidly without additional hard- or software and linear measurements of the brain stem in adults have been made. [16,17]There are many studies in the literature where anatomical structures in brain are measured quantitatively in terms of volume, width and length [18]. Investigations of aging effects on the brain stem are important, not only to understand normal aging, but also for comparative study of the pathophysiology of degenerative brain disorders. Several studies have focused on structural changes in the midbrain that contains nuclei which are important for voluntary or involuntary movements and also nerve fibers conducting sensory and motor information. [19, 20]

Sex differences in gross posterior fossa neuroanatomy have been reported in several studies. [21-24] Hayakawa et al. studied the relation between the pons and age.[25] MRI studies have correlated midbrain morphology with symptomatology in several disorders [26,27], suggesting that morphometric data may indirectly reflect underlying neurochemical or pathologic process. Coffman et al. [28] found no differences between schizophrenics and controls. For further depiction the gender differences and effects of age on brain stem structures; we examined the two potential sources of normal variability in regional brain stem: age and gender. The outcome of this study provide a valuable addition to the normative database of the brain stem

anatomy using simple linear MRI morphometric study in that they support the concept of differential aging and gender impact on the norms of mid brain, pons, medulla oblongata**.**

II. Samples and Methods

This is a retrospective cross section study, conducted at Alhada Military hospital and King Faisal Hospital in Taif City, KSA in Radiology Department during period from June 2014 to April 2017.

1.1 Sample:

The study sample including: 275 patients; 126(45.8%) were females and 149(54.2%) were males, were referred for MRI, their MRI findings were normal brain and posterior fossa anatomical structures. No patient had a medical history or clinical examination suggesting intracranial abnormality. MRI was performed after informing the patients about the procedure of the examination. The age and gender of the patients were registered in the data collection sheet. All MRI brain cases with abnormal appearance were excluded.Participants' ages were <10>60years old, their mean age was 36.33 ±23.75 years old (max=91.00years, min=1.00 years). Ages <10 were41(14.9%), 11-20 were 43(15.6%), 21-30 years were 38(14.2%), ages between 31-40 years were35(12.7%),41-50 were 35(12.7%),51-60 were 32(11.6%) and ages >60 were 50(18.2%) All the patients were examined using MRI machine GE Optima MR450W, 1.5 Tesla and Skyra Siemens AG 2012, 3 Tesla, version: syngo MRD13. Protocol used was: T1 sagittal image, 5 mm thick with a gap of 1 mm were obtained with the spin- echo (SE) sequence.

1.2 Methods:

Linear measurement was done in (cm): - **Mid brain**: The sagittal diameter of the midbrain was measured across the midbrain to the tectum. - **Pons**: The pons diameter was measured mid- point between its upper and lower borders and perpendicular to its long axis to the fourth ventricle.- **Medulla Oblongata**, the anteroposterior diameter perpendicular to the longitudinal axis was measured just above the posterior kink at the cervicomedullary junction**.**

III. Tables And Figures

Table No (1) Brain Stem measurements done in 275 patients**.**

Descriptive Statistics					
	N	Min	Max	Mean	Std. Deviation
Midbrain diameter (cm)	275	.90	2.60	1.54	0.19
Pons diameter (cm)	275	1.30	2.80	2.24	0.22
Medulla oblongata diameter (cm)	275	.30	1.70	1.33	0.14

Table No (2) Brain Stem measurements done in 275 patients classified according to age**.**

Descriptive							
		N	Mean	Std. V	Min	Max	P-value
Midbrain diameter (cm)	<10	41	1.36	.22	.90	2.00	0.000
	11-20	43	1.60	.15	1.20	1.90	
	21-30	39	1.59	.14	1.30	1.90	
	31-40	35	1.64	.14	1.30	1.90	
	41-50	35	1.62	.13	1.40	1.90	
	51-60	32	1.59	.22	1.20	2.60	
	60+	50	1.46	.18	1.00	1.90	
	Total	275	1.54	.19	.90	2.60	
Pons diameter (cm)	<10	41	1.96	.27	1.30	2.80	0.000
	11-20	43	2.20	.16	1.90	2.50	
	21-30	39	2.28	.14	2.00	2.60	
	31-40	35	2.32	.18	1.90	2.70	
	41-50	35	2.32	.19	1.80	2.70	
	51-60	32	2.35	.14	2.10	2.60	
	60+	50	2.32	.16	2.00	2.70	
	Total	275	2.24	.22	1.30	2.80	
Medulla oblongata diameter (cm)	<10	41	1.17	.18	.30	1.40	0.000
	11-20	43	1.34	.11	1.10	1.60	
	21-30	39	1.35	.07	1.20	1.60	
	31-40	35	1.37	.13	1.20	1.70	
	41-50	35	1.36	.12	1.20	1.60	
	51-60	32	1.36	.09	1.20	1.60	
	60+	50	1.35	.11	1.20	1.70	
	Total	275	1.33	.14	.30	1.70	

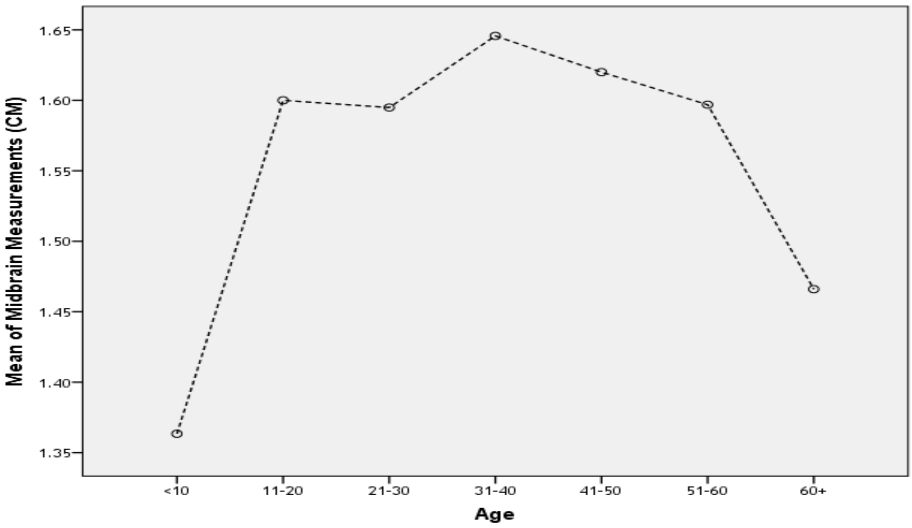

Figure (1) Mean diameter of mid brain (cm) measured in various age groups

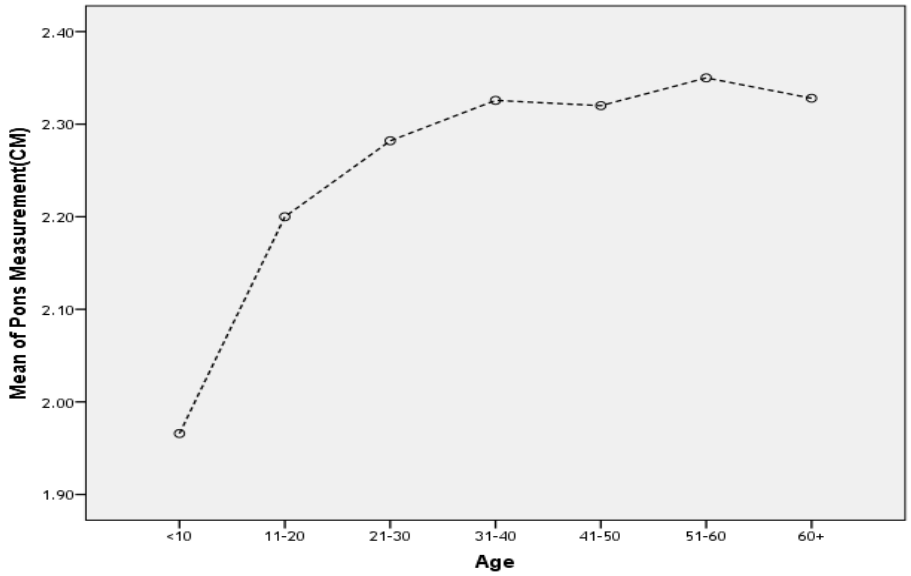

Figure (2) Mean diameter of pons(cm) measured in various age groups

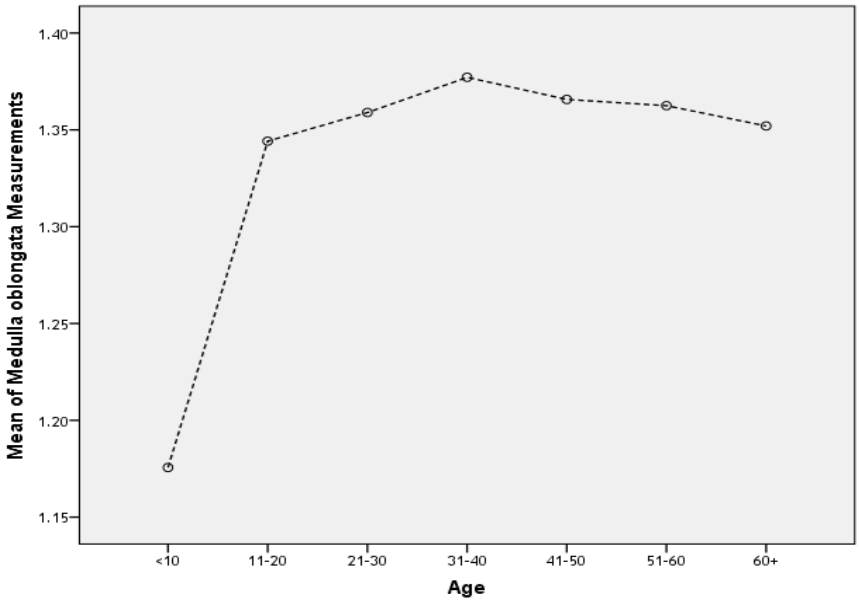

Figure (3) Mean diameter of medulla oblongata (cm) measured in various age groups

IV. Discussion

In this study, we have demonstrated the age and gender effect of brainstem using simple linear diameter MRI method. The measurements were obtained in Saggital planes for mid brain,pons and medulla ablongata as presented in table(1).The increasing age showed significant reduction on the brain stem measurement at p =0.000 for mid brain, pons and medulla oblongata, table (2)

Previous studies examining age-related decline in the brainstem [8,9] and significant midbrain measurements reduction [24]. This had previously been attributed to shrinkage of the substantia nigra [29], our study agrees with previous work in that brainstem aging-associated degeneration seems to be confined to the midbrain. However, our results indicate that it is mainly the reduction of the measurement may be due to the loss of the superior cerebellar fiber bundles (brachium conjunctivum, fasciculus cerebello thalamicus [30] as mentioned in previous is that those anatomical structures are responsible for this finding.

Our results disagree with previous studies in the study concerning the pons and medulla that don't show measurement loss in aging [31, 9].

Data on age-related changes of the brain stem in normal subjects will facilitate further investigation of the relation between brain stem changes and the neuromotor decline with normal aging. This normative data can also be used to compare the findings in patients with neurologic disorders such as Parkinson disease, Alzheimer disease and schizophrenia. This study may support the findings on morphometrical sex differences and age-related changes. However, discrepancies in the results concerning the age-related changes in the brain stem remains speculative, though some authors suggest a selective vulnerability of specific posterior fossa structures to the effects of aging and sex.

The impact of gender was also been studied, table (3) with no significant relation between the gender and brain stem measurements. A few groups have reported on aging of the brain stem. One study is in consistent to our results; Doraiswamy et al. [32] reported that the measurements of the midbrain decline with age in both sexes, but found no differences between men and women. Also similar results with significant decline in the midbrain measurement were reported by Shah et al. [22], Oguro et al. [33] and Sohmiya et al. [34].

The current study showed that the mid brain decline in the measurements at saggital plane by 3mm at the age >50years and by 13mm as the age increased >60years old it could be accounted for in part by neuronal death or degeneration with nuclei and/or tracts of the midbrain. As mentioned by Shah et al. [22]

As well significant increasing in the pons was detected in the ages above 50years and decline by 0.03 thereafter at the age above 60 years; similarly Raininko et al. [35] found minimal reduction in the midsagittal diameter of the midbrain and pons after the age of 50 years, but no sex differences in linear measurements. Mc Geer et al. [36] have reported a decrease in the number of neurons in the substantia nigra between the age of 20 and 80. Reduction in the medulla obliongata was observed at the ages 41-50 and 51-60 years (figures1,2,3) reverse findings were reported by Oguro et al. [33], to be non-significant age-related changes in the mid-sagittal area of pons, but similar findings for pons and medulla oblongata were reported by Shah et al. [22,37].

Further studies on the assessments of sex differences and age-related changes in the brain stem parts (midbrain, pons and medulla oblongata) and their correlations with midsagittal supra tentorial anatomical structures should be planned for collecting data in large sample size and at different races and ethnic groups.

Imaging modalities were used to characterize the brain structural anatomy. Methods for measuring the pons on CT, and that of the mesencephalon on MRI have been described, and normal values for adults were recorded. [15, 16]Volumetric studies are too time-consuming for routine work; volume and area measurements are not possible using the software of some MR imagers; our application to the simple linear measurements made it rapidly evaluated without additional hard or software, similarly linear measurements of the brain stem in adults have been made. [16,17]as well many studies took place where anatomical structures in brain are measured quantitatively in terms of volume, width and length [18]

There are several studies move towards the set of population-based measures of brain structure neuroimaging as well; advances in MRI scanner technology are making it possible to obtain very high-resolution structural data allowing the characterization in term of shape, symmetry, and complexity.[38] With advances in neuroimaging and for further studies regarding the brain; recommendation to consider the trajectories; may organize the groundwork for the next stages of exploring the influences of age and gender on those arcs and ultimately using the knowledge to optimize brain/brain stem development in healthy and clinical cases.

V. Conclusion and recommendations

MRI is an excellent imaging method in the characterization of brain stem, the used simple linear measurements made it suitable for routine work during practice and the criteria allowing definition of norms and reduction changes of the brain stem on a routine basis by aging .The normal ranges (in the ages between <10>60 for both genders) given in this study can be acknowledged for the assessment of changes in cases of suspected neurodegenerative disorders.

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