



## AGE RELATED CHANGES IN CORPUS CALLOSUM

Kavita Nanda

Assistant Professor, Department of Anatomy, Dr. RKGMC Hamirpur (H.P.)

Anupam Nanda\*

Assistant Professor, Department of Surgery, Dr. RKGMC, Hamirpur(H.P.)  
\*Corresponding Author

Vishal Kalia

Assistant Professor, Department of Anatomy, Dr RPGMC, Tanda (H.P.)

## ABSTRACT

**INTRODUCTION:-** This quantitative MRI study done on 100 healthy adult individuals between 20-60 years of age reports measurement of different dimensions of corpus callosum and any changes in the dimensions with ageing.

**METHODS:** MRI of corpus callosum of adult healthy individuals aged between 20-60 years were done and morphometric measurements of different parameters i.e. length, width, height and subregions of corpus callosum were noted and compared.

**RESULTS:** In our study it was found that-

1. Thickness of splenium, thickness of posterior part of corpus callosum & shortest distance from posterior most point of corpus callosum to cortical surface (P-S) increased with age.
2. Length of corpus callosum, length of corpus callosum/length of brain increased upto 39 years and thereafter declined.
3. Height of corpus callosum, thickness of body at mid-point, maximum thickness of the body and minimum thickness started to decrease after 50 years.

**CONCLUSION:** The results of this study indicate that ageing effects are more pronounced in genu and anterior part of corpus callosum.

**KEYWORDS :** Corpus callosum, MRI, Normal Ageing

## AIMS AND OBJECTIVES:

To study the variation in the size of corpus callosum with advancing age.

## INTRODUCTION:

The corpus callosum is a prominent body of white matter that connects the two cerebral hemispheres in a homotropic manner with reference to cortex. Corpus callosum is readily visualised on MRI<sup>1</sup>. The midsagittal section of corpus callosum on MRI can be used to measure its dimensions in different subregions & this procedure can be employed to estimate normative ageing process. Most cross-sectional MRI studies proves corpus callosum to be a relatively immune to age-related shrinkage upto seventh decade of life<sup>(2-7)</sup> on the contrary, some studies have shown senescent effects.<sup>(8-11)</sup>

## MATERIAL AND METHODS

This study was carried out in dept of Anatomy, Surgery and Radiology at Dr.RKGMC, Hamirpur and Dr.RPGMC, Tanda. A total of 100 healthy individuals aged between 20-60 years were included in the study and their dimensions of corpus callosum and its subregions on MRI Scans were noted. Individuals were further subdivided into 4 age groups i.e. 20-29 years, 30-39 years, 40-49 years and 50-59 years for comparison.

## THE FOLLOWING SETS OF MEASUREMENTS WERE TAKEN

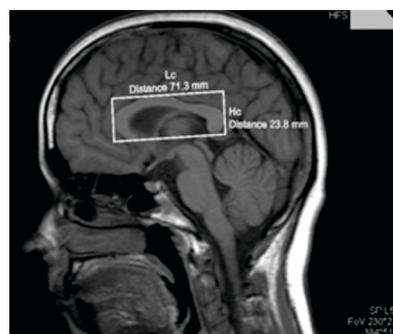
1. Length of corpus callosum (Lc).
2. Thickness of body of corpus callosum at mid point (T).
3. Maximum thickness of rostrum (Tr).
4. Maximum thickness of splenium (Ts).
5. Height of corpus callosum (Hc).
6. Maximum and minimum thickness of body of corpus callosum (Tmax and Tmi).
7. Maximum thickness of anterior half of corpus callosum body (TBA).
8. Maximum thickness of posterior half of corpus callosum body (TBP).
9. Genu-Fornix Length (G-F): Distance between anterior edge of genu to anterior edge of columns of fornix.
10. Genu-Anterior Commissure Length (G-C): Distance

between anterior edge of genu to anterior edge of anterior commissure.

11. Shortest distance from anterior most point of corpus callosum to cortical surface (A-S)
12. Shortest distance from top most point of corpus callosum to cortical surface (T-S).
13. Shortest distance from posterior most point of corpus callosum to cortical surface (P-S).
14. Length of brain (LB): From frontal pole to occipital pole of brain in midsagittal section.
15. Distance from frontal pole of brain to anterior most point of corpus callosum (F-A).
16. Distance from occipital pole of brain to posterior most point of corpus callosum (O-P).

## RATIOS

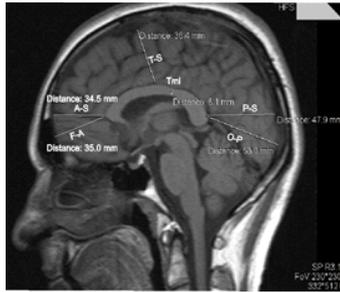
17. Length of corpus callosum /Length of brain (Lc/LB).
18. Splenial thickness /Length of corpus callosum (Ts/Lc).
19. Splenial thickness /Length of brain (Ts/LB).
20. Thickness of body at mid point/Length of corpus callosum (T/Lc).
21. Thickness of body at mid point/Height of corpus callosum (T/Hc).



**Fig.1.MEASUREMENT OF CALLOSUM (MIDSAGITTAL MRI)**

Lc: Length of corpus callosum

Hc: Height of corpus callosum



**Fig. 2: MEASUREMENT OF CORPUS CALLOSUM (MIDSAGITTAL MRI)**

A-S: Shortest distance from anterior most point of corpus callosum to cortical surface  
 F-A: Distance from frontal pole of brain to anterior most point of corpus callosum  
 T-S: Shortest distance from top most point of corpus callosum to cortical surface  
 Tmi: Minimum thickness of body of corpus callosum  
 P-S: Shortest distance from posterior most point of corpus callosum to cortical surface  
 O-P: Distance from occipital pole of brain to posterior most point of corpus callosum.

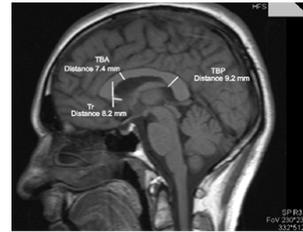


**Fig. 3: MEASUREMENT OF CORPUS CALLOSUM (MIDSAGITTAL MRI)**

G-F: Genu-Fornix Length  
 G-C: Genu-Anterior Commissure Length  
 T: Thickness of body of corpus callosum at mid point  
 Ts: Maximum thickness of splenium

**COMPARISON BETWEEN VARIOUS AGE-GROUPS**

CC Para Meter	20-29 (N= 30)		30-39 (N= 20)		40-49 (N= 35)		50-60 (N= 15)		F; P value
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	
Lc	7.039	0.5667	7.3085	0.4930	7.0977	0.4909	7.012	0.6042	1.279; 0.286
Hc	2.310	0.6649	2.4235	0.6248	2.5566	0.6540	2.442	0.5297	0.817; 0.488
T	0.6043	0.1359	0.601	0.1451	0.6723	0.1582	0.6227	0.1102	1.636; 0.186
Tmax	0.8227	0.1409	0.811	0.1609	0.894	0.1855	0.7433	0.0789	3.629; <b>0.016**</b>
Tmi	0.4197	0.0862	0.4705	0.1298	0.4869	0.1091	0.4587	0.0472	2.510; 0.063
-[Tr	3.5273	0.2687	1.078	0.1671	1.0823	0.2170	1.1013	0.2043	0.712; 0.547
Ts	1.087	0.1851	1.095	0.1914	1.0991	0.1975	1.128	0.2169	0.150; 0.929
Tba	0.7903	0.1671	0.7305	0.1243	0.8394	0.2496	0.668	0.1121	3.420; <b>0.020**</b>
Tp	0.7193	0.1307	0.7195	0.2286	0.806	0.2133	0.65	0.0821	3.018; <b>0.034**</b>
G-F	2.4317	0.4122	2.665	0.3565	2.5563	0.4628	2.872	0.3403	4.130; <b>0.008**</b>
G-C	2.6683	0.3252	2.8275	0.2345	2.7331	0.3164	2.7293	0.2774	1.133; 0.340
A-S	3.3157	0.3366	3.464	0.4157	3.3214	0.3393	3.2953	0.2347	1.039; 0.379
P-S	4.1757	0.3602	4.4185	0.5137	4.5111	0.4707	4.5587	0.5742	3.558; <b>0.017**</b>
T-S	3.568	0.3470	3.7505	0.5660	3.7246	0.4395	3.5273	0.2687	1.535; 0.210
LB	15.4223	0.7792	15.8365	0.8177	15.5151	0.9041	15.768	1.1277	1.151; 0.333
F-A	3.5107	0.3679	3.436	0.4278	3.5426	0.4055	3.4793	0.4894	0.303; 0.823
O-P	5.3643	0.5763	5.535	0.6627	5.6486	0.5358	5.552	0.6234	1.275; <b>0.287**</b>
Lc/LB	0.4567	0.0331	0.4614	0.0181	0.4583	0.0338	0.4454	0.0345	0.836; 0.477
Ts/Lc	0.1543	0.0222	0.1497	0.0230	0.1546	0.0239	0.1626	0.0391	0.705; 0.551
Ts/LB	0.0706	0.0122	0.0691	0.0114	0.0710	0.0129	0.0718	0.0144	0.148; 0.931
T/Lc	0.0862	0.0197	0.0820	0.0184	0.0950	0.0224	0.0899	0.0210	1.949; 0.127
T/Hc	0.2796	0.0942	0.2530	0.0474	0.2737	0.0765	0.2639	0.0662	0.548; 0.651



**Fig. 4: MEASUREMENT OF CORPUS CALLOSUM (MIDSAGITTAL MRI)**

TBA: Maximum thickness of anterior half of corpus callosum body  
 Tr: Maximum thickness of rostrum  
 TBP: Maximum thickness of posterior half of corpus callosum body

**STATISTICAL ANALYSIS-**

Post-Hoc test, a variant of ANOVA test was used to do the comparison between these age groups. ANOVA was applied to do comparison amongst all groups.

**RESULTS-**

In our study following results were observed:

1. Ts, P-S and Tp increased with increase in age.
2. Hc and thickness of anterior part of corpus callosum (Tba) declined after 50 years of age.
3. Length of corpus callosum (Lc) decreased steadily after 40 years of age.
4. Mean difference of Tba between age groups 40-49 years and 50-60 years was  $0.17143 \pm 0.058$  which was statistically significant with a 'p' value of 0.020.
5. Mean difference of Tp between 40-49 yrs and 50-60 yrs was  $0.1560 \pm 0.05572$  which was statistically significant with a 'p' value of 0.031.
6. Mean difference of G-F between age groups 20-29 yrs and 50-60 yrs was  $-0.44033$  with a 'p' value of 0.006 which was statistically significant.
7. Mean difference of P-S between age groups 20-29 yr and 40-49 yr was  $-0.33548 \pm 0.11616$  with a 'p' value of 0.024 which was statistically significant.
8. Mean difference of P-S between age groups 20-29 years and 50-60 years was  $-0.38300 \pm 0.14764$  with a 'p' value of 0.053 which was statistically significant.

**DISCUSSION-**

Results of different studies done on the size changes of corpus callosal with ageing are equivocal. Studies conducted by Pfefferbaum et al<sup>(6)</sup>, Pozzilli et al<sup>(12)</sup>, Johnson SC et al<sup>(5)</sup> concluded that age related thinning of corpus callosum is modest whereas Sullivan et al<sup>(13)</sup>, Weis et al<sup>(9)</sup> and Doraiswamy et al<sup>(8)</sup> reported statistically significant changes. Salat D et al<sup>(11)</sup> and Weis et al<sup>(9)</sup> reported greater vulnerability in size changes with advancing age in anterior than posterior regions of corpus callosum that is similar to our findings. Weis et al<sup>(9)</sup> reported significant decrease in size of genu and anterior part of trunk of corpus callosum with age suggesting alteration in frontal and temporal interhemispheric fibre system. Corpus callosum is located adjacent and superior to lateral ventricle, these changes may be attributed to expansion of lateral ventricle in elderly.<sup>(11,13)</sup> Decrease in corpus callosal size may reflect histological changes in cerebrum, such as the loss of synaptic connections and callosal collaterals.

Study conducted by Mori et al<sup>(14)</sup> in 2005 concluded that MR Diffusion Tensor Imaging(DTI) enables examination of white matter tracts and markers of white matter microstructural integrity at macroscopic resolution in living human beings by measuring Water Diffusion. Assaf and Pasternak<sup>(15)</sup> in 2008 conclude that Fractional Anisotropy (FA) and Diffusivity (D) are useful in measuring microstructural integrity.

Advanced age is associated with increased occurrence of myelin sheath deformations<sup>(16,17)</sup> fewer small-diameter myelinated fibers<sup>(18,19)</sup> expanded extra-axonal spaces, and loss of anterior commissural fibres, but not with axonal degeneration<sup>(20,21)</sup>. Age related white matter differences like increased axonal diameter and reduced packing density could result in increased diffusivity and reduced FA. Although myelin influences both FA and RD<sup>(22,23)</sup> these indices are poor proxies for local myelin content<sup>(24,25,26,27)</sup>. Axonal diameter, independent of myelination, appears the strongest anatomical correlate of AD<sup>(24)</sup>.

In 2007, Sullivan and Pfefferbaum<sup>(28)</sup> found that advancing age is associated with reduction in FA on DTI studies. Study conducted by O'Sullivan et al<sup>(29)</sup> in 2001 concluded that integrity of Corpus callosal white matter reduces with advancing age which is usually greater in anterior compared to posterior brain regions. Study conducted by Bastin et al<sup>(30)</sup> supported the "Frontal Aging Hypothesis" as there was significant positive correlation between Mean Diffusivity (D) and age in genu and negative correlation between FA and age in splenium. These results are similar to our finding where thinning of anterior part of corpus callosum was observed after 50 years of age. Some changes in shape of splenium were mediated by age related global brain atrophy and ventricular enlargement. In 2016, Vanessa et al<sup>(31)</sup> found age related metabolic and microstructural vulnerability of splenium as there was decrease in N-Acetylaspartate and T2 and increase in T2 with advancing age. On the contrary, in our study it was found that splenium thickness increased with age upto 60 years. In contrary study conducted by Bender et al<sup>(32)</sup> in 2015 observed no significant differences in size change for genu or splenium with advancing age.

**CONCLUSION**

The results of this study indicate more pronounced ageing effects in genu and anterior part of corpus callosum with advancing age.

**REFERENCES**

- Pandya DN, Seltzer B. The topography of commissural fibres. In: Lepore F, Piito M, Jasper HH, eds. Two Hemispheres-One Brain: Functions of corpus callosum. New York: Alan R. Liss, Inc, 1986: 47-74
- Beigon A, Eberling JL, Richardson BC, Roos MS, Wong STS, Reed BR, Jagust WJ. Human Corpus Callosum in Aging and Alzheimer's disease: A Magnetic Resonance Imaging Study. *Neurobiol Aging* 1994;15: 393-397

- Cowell PE, Allen LS, Zalaito NS. A developmental study of sex and age interactions in human corpus callosum. *Dev Brain Res* 1992; 66: 187-92
- Dreisen NR, Raz N. The influence of sex, age and handedness on corpus callosum morphology: a meta analysis. *Psychobiol* 1995; 23: 240-47
- Johnson SC, Farnworth T, Pinkston JB, Bigler ED, Blatter DD. Corpus callosum surface area across the human adult life span: effect of age and gender. *Brain Res Bull* 1994; 35: 373-77
- Pfefferbaum A, Lim KO, Desmond J, Sullivan EV. Thinning of corpus callosum in older alcoholic men: a magnetic resonance imaging study. *Alcohol Clin Exp Res* 1996; 20: 752-57
- Thompson P, Narr KL, Blanton RE, Toga AW. Mapping Structural Alterations of the Corpus Callosum. During Brain Development and Degeneration. In : Zaudel E, Tacoboni M, eds. Proceedings of the NATO ASI on the corpus callosum. New York: Kluwer Academic Press 2000, in press.
- Doraiswamy PM, Figiel GS, Husain MM. Aging of the human corpus callosum magnetic resonance imaging in normal volunteers. *J Neuropsychiatr Clin Neurosci* 1991; 3: 392-97
- Weis S, Kimbacher M, Wenger E, Neuhold A. Morphometric analysis of corpus callosum using MR: Correlation of measurement with aging in healthy individuals. *Amer J Neuroradiol* 1993; 14: 637-45
- Davatzikos C, Resnick SM. Sex differences in Anatomic measures of interhemispheric connectivity: Correlation with cognition in women but not men. *Cerebral cortex* 1998; 8: 635-40
- Salat D, Ward A, Kaye IA, Janowsky JS. Sex differences in the corpus callosum with ageing. *Neurobiology of ageing* 1997; 18: 191-97
- Pozzilli C, Bastimello S, Bozzao A, Pierallini A, Guibilei F, Argentino C et al. No differences in corpus callosum size by sex and aging. A quantitative study using magnetic resonance imaging. *J Neuroimaging* 1994; 4(4): 218-221
- Sullivan EV, Pfefferbaum A, Adalsteinsson E, Swan GE, Carmelli D. Differential rates of regional brain change in callosal and ventricular size: A four year longitudinal MRI study of elderly men. Oxford University Press, 2002: 438-45
- Mori S, Wakana S, Nagae PZ, Zijden V, PCM. MRI Atlas of Human White Matter. Amsterdam: Elsevier, 2005
- Assaf Y, Pasternak O. Diffusion Tensor Imaging(DTI)- based white matter mapping in Brain Research: A review *Journal of Molecular Neuroscience: HN* 2008; 34(1): 51-61
- Bowley MP, Cabral H, Rosene DL, Peters A. Age changes in Myelinated Nerve fibres of the Cingulate Bundle and Corpus Callosum in the Rhesus Monkey. *The Journal of comparative Neurology*. 2010; 518(15): 3046-3064
- Peters A. The effects of normal aging on myelin and nerve fibres: a review. *J Neurocyt*. 2002; 31: 581-593
- Marnier L, Nyengaard JR, Tang Y, Pakkenberg B. Marked loss of myelinated nerve fibres in Human Brain with age. *The journal of comparative neurology*. 2003; 462(2): 144-152
- Tang Y, Nyengaard JR, Pakkenberg B, Gundersen HJ. Age-induced white matter changes in the human brain: a stereological investigation. *Neurobiol Aging*. 1997; 18(6): 609-615
- Budde MD, Xie M, Cross AH, Song SK. Axial diffusivity in the primary correlate of axonal injury in the experimental autoimmune encephalomyelitis spinal cord: a quantitative pixelwise analysis. *J Neurosci*. 2009; 29(9): 2805-13
- Nielson K, Peters A. The effects of aging on the frequency of nerve fibres in rhesus monkey striate cortex. *Neurobiol Aging*. 2000; 21(5): 621-28
- Song SK, Sun SW, Ramsbottom MJ, Chang C, Russell J, Cross AH. Demyelination revealed through MRI as increased radial (but unchanged axial) diffusion of water. *Neuroimage*. 2002; 17(3): 1429-1436.
- Sun SW, Liang HF, Cross AH, Song SK. Evolving Wallerian degeneration after transient retinal ischemia in mice characterized by diffusion tensor imaging. *Neuroimage*. 2008; 40(1): 1-10.
- Beaulieu, C. The biological basis of diffusion anisotropy. In : Johansen-Berg, H.; Behrens, TE., editors. *Diffusion MRI: From quantitative measurements to In vivo neuroanatomy*. Academic Press: 2012. p. 106-26.
- De Santis S, Drakesmith M, Bells S, Assaf Y, Jones DK. Why diffusion tensor MRI does well only some of the time: variance and covariance of white matter tissue microstructure attributes in the living human brain. *Neuroimage*. 2014; 89: 35-44.
- Kolind SH, Laule C, Vavasour IM, Li DKB, Trabousee AL, Madler B, et al. Complementary information from multi-exponential T2 relaxation and diffusion tensor imaging reveals differences between multiple sclerosis lesions. *Neuroimage*. 2008; 40(1): 77-85.
- Madler B, Drabycz SA, Kolind SH, Whittall KP, MacKay AL. Is diffusion anisotropy an accurate monitor of myelination? Correlation of multicomponent T2 relaxation and diffusion tensor anisotropy in human brain. *Magn Reson Imaging*. 2008; 26(7): 874-888.
- Sullivan EV, Pfefferbaum A. A neuroradiological characterization of normal adult aging. *The British Journal of Radiology*. 2007; 80 (spec No 2): S99-S108
- O'Sullivan M, Jones OK, Summers PE, Morris RG, Williams SCR, Markus HS. Evidence of cortical "disconnection" as a mechanism of age related cognitive decline. *Neurology*. 2001; 57(4): 632-638
- Bastin ME, Maniega SM, Ferguson KJ, Brown LJ, Wardlaw JM, Mac Lullich AMJ, Clayden JD. Quantifying the effects of Normal Aging on White Matter Structures using Unsupervised Tract Shape Modelling. *Neuroimage*. 2010 May 15; 51(1): 1-10
- Elyers VV, Maudsley AA, Bronzlik P, Dellani PR, Lanfermann H, Ding XQ. Detection of normal aging effects on human brain metabolite concentrations and microstructure with whole brain MR imaging and quantitative MR imaging. *Am J Neuroradiol*. 2016 march; 37(3): 447-454
- Bender AR, Raz Naftali. Normal-Appearing Cerebral White Matter in Healthy Adults: Mean Change over Two Years and Individual Differences in Change. *Neurobiol Aging*. 2015 May; 36(5): 1834-1848