The effect of aging and gender on the size of the corpus callosum with and without Down syndrome: a radiological study

Abdullah. G. Alkushi

Department of Anatomy, Faculty of Medicine, Umm Al-Qura University, Saudi Arabia
dr.alkushi@gmail.com

Abstract: It is important to have normative values for morphometric measurements of the corpus callosum (CC) according to sex, age and certain diseases. No documented data exist regarding the anatomical characteristics of the CC in Down syndrome patients. Thus, this magnetic resonance imaging (MRI) study was performed to provide an overview of the effect of age and sex on the size of the CC in Saudi Arabian individuals with and without Down syndrome. The longitudinal and vertical length of the brain and CC were measured using MRI of a midsagittal section of 100 normal subjects (50 males, 50 females) and 50 Down syndrome patients (25 males, 25 females). Our work divided into five age groups: from 1 until 6 years, from 6 to less than 12 years old, from 12 to less than 18 years old, from 18 to less than 30 years old and 30 years or older. The diameters of the brain and CC were significantly longer in normal individuals than in Down syndrome patients. The diameters of CC, longitudinal diameter of the genu and length of the splenium were larger in males than in females, but these differences were not significant. The diameters of the brain were significantly longer in males than in females. This study showed that various parameters in Down syndrome patients vary with the values documented in the normal population.
[Abdullah. G. Alkushi. **The effect of aging and gender on the size of the corpus callosum with and without Down syndrome: a radiological study.** *Life Sci J* 2018;15(1):86-91]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). http://www.lifesciencesite.com. 15. doi:10.7537/marslsj150118.15.

Keywords: Gender; Down syndrome; MRI; Aging

1. Introduction

The human corpus callosum (CC) is the largest and most prominent and important anatomical functional commissure between the two hemisphere in the brain. The CC provides neural communications between the activities of both cerebra and has a unique structure with a geometric arrangement (Mourgela et al., 2007).

The activities of the frontal cortex of both cerebra and their neural communications are controlled by the genu and rostrum. Additionally, most of the motor and primary sensory cortex in both hemispheres coordinates via the body of the CC, while the fibers of the other lobes cross the CC through the splenium. The CC plays a role in behavior, memory, learning and some cognitive functions (Paul et al., 2003; Quigley et al., 2003).

Multiple studies have reported that CC morphology and size may change due to various diseases (Yasar et al., 2006), such as Alzheimer's disease (AD) (Teipel et al.,2002; Head et al., 2016), leukoaraiosis (Yamauchi et al., 2000), Williams's syndrome (Tomaiuolo et al.,2002), dyslexia (von Plessen et al., 2002), Tourette's syndrome (Plessen et al., 2004), Down syndrome (DS) (Teipel et al., 2003), depression (Lacerda et al., 2005), schizophrenia (Narr et al., 2002) and HIV (Thompson et al., 2006).

The sizes of different organs, including the CC, differ according to race/ethnicity in different areas in the world, and the identified differences in CC size and morphology is an area of interest to researchers (Mourgela et al., 2007; Peterson et al., 2001).

Additionally, Bermudez and Zatorre, (2001) found a significant difference in the size and morphology of the CC between genders. However, Luders *et al.* 2006 did not find a significant difference in their study.

The CC appears in the midline sagittal section of the adult brain as an arch of white matter approximately 10 cm in size; its anterior part is 4 cm, and its posterior part is 6 cm (Standring and Crossman, 2005).

Anatomists and neuroradiologists have frequently faced a problem regarding the lack of a collective documented quantitative reference of the size of the normal CC for different ages and genders. Moreover, little is known about changes in the size and tissue characteristics of its sub-regions in different age groups (Keshavan et al., 2002).

It has been found that the longitudinal diameter of the CC is larger in males, and the anterior part of the CC reduces with age due to atrophic changes in the hemispheres (Gupta et al., 2008; Suganthy et al., 2003). Other findings showing sex differences in CC morphology across the lifespan (Prendergast et al., 2015) and development changes in CC observed in early of life (Tanaka-Arakawa et al., 2015).

Morphological features of selected DS patients

Typical features in an individual with DS include short stature and obesity with a small, rounded head

(microcephaly and brachycephaly), flattened occipital bone and sloping forehead. In infants, the fontanels are large and slow to close. Radiologic examination may reveal hypoplasia of the maxillary sinuses and absence of the sphenoidal and frontal sinuses. The nasal bones are hypoplastic with a flattened nasal bridge in the face is characteristic, with a rounded shape (Head et al., 2016).

Individuals with DS develop a clinical syndrome of Alzheimer disease that has almost identical neuropathological characteristics to those of non-DS patients with Alzheimer disease (AD) (Lacerda et al., 2005).

The main difference is the earlier age of onset in DS individuals (Mann, 1988).

No documented data exist regarding the anatomical characteristics of the brain and CC in DS patients; therefore, this study was performed to measure the differences in these dimensions relative to normal subjects.

2. Material and Methods

This descriptive study was conducted on 150 subjects, including 75 males and 75 females, aged 1 to 45 years, from February2016 to June2016, who had normal magnetic resonance imaging (MRI) findings. All participants provided informed consent. The study included100 normal subjects (50 males, 50 females) and 50 DS patients (25 males, 25 females), ascertained by karyotyping.

The subjects were chosen from the MRI scanning unit of the radiology department according to a chronic headache survey and mild delayed milestones of growth. The inclusion criteria consisted of no cerebrovascular lesions, tumor or head accidents or history of neurological disease.

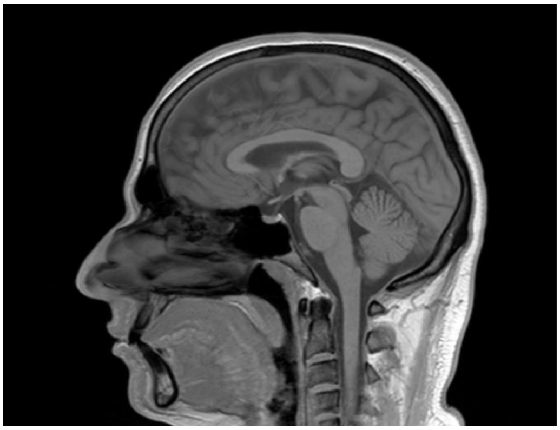

Fig 1: 31 year old Saudi Male mid-sagittal brain MRI.

The subjects were divided into five age groups, including group 1 (less than 6 years old), group 2 (from 6 to less than 12 years old), group 3 (from 12 to less than 18 years old), group 4 (from 18 to less than 30 years old) and group 5 (30 years or older). The size of the brain and CC were measured. MRI was performed using a mid-sagittal view of the cerebral hemispheres (figure 1 and figure 2).

The following diameters were measured:

CCAP: Length of the CC from the most anterior to the most posterior point, passing through the point of maximal curvature of the inner border of the genu (figure 3).

BAP: Longitudinal diameter of the brain between the most anterior and most posterior points of the cerebral hemisphere at the level of the CC (figure 4).

FG: From the genu of the CC to the frontal pole of the brain (figure 4). SO: From the splenium of the CC to the occipital pole of the brain (figure 4).

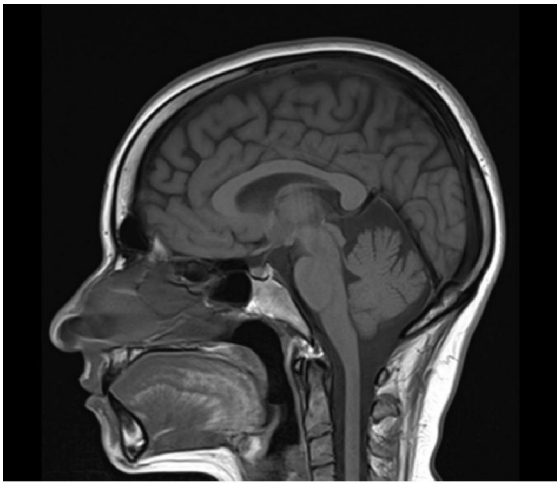

Fig 2: 31 year old Saudi Female mid-sagittal brain MRI.

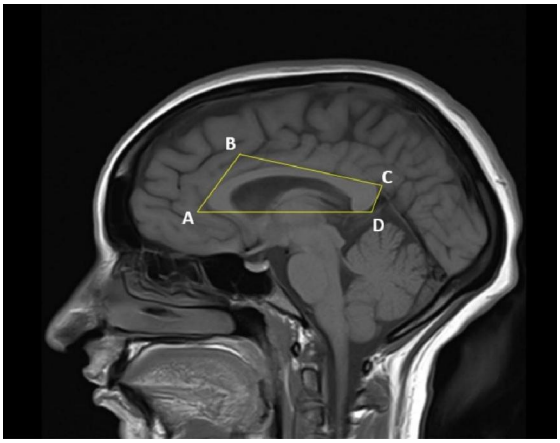

Fig. 3 Measurements of corpus callosum (CC) length (A, B, C, D) from the most anterior to the most posterior point, passing through the point of maximal curvature of the inner border of the genu (CCAP).

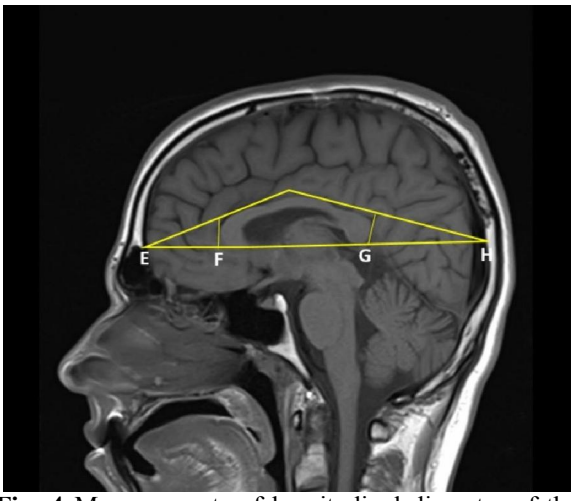

Fig. 4 Measurements of longitudinal diameter of the brain between the most anterior and most posterior points of the cerebral hemisphere at the level of the CC from E to H (BAP), from the genu of the CC to the frontal pole of the brain from E to F (FG), from the splenium of the CC to the occipital pole of the brain from G to H (SO).

Statistical analysis

We present descriptive statistics, standard deviations, ANOVA and a critical test of significance.

3. Results

Age-related differences

The mean value of BAP from the medial aspect showed a significant increase in first 3 age groups. These findings appeared as a slopping increase until a plateau was reached, while the insignificant increase in the last 2 groups exhibited a linear appearance.

13.16 ± 0.039 cm in group 1 normal,12.86± 0.102 cm in group1 DS

14.73 ± 0.024 cm in group 2 normal,14.16± 0.063cm in group2 DS

16.01 ± 0.049 cm in group 3 normal,15.82± 0.089 cm in group3 DS

16.34 ± 0.045 cm in group 4 normal,16.14± 0.076 cm in group4 DS

16.44± 0.077 cm in group 5 normal, 15.71± 0.033 cm in group5 DS

The mean value of CCAP showed a statistically significant increase from group 1 to group3. These findings appeared as a slopping increase until a plateau was reached, while the insignificant increase in the last 2 groups had a linear appearance.

6.56 ± 0.039 cm in group 1normal, 6.16 ± 0.082 cm in group1 DS

7.03± 0.044 cm in group 2 normal, 6.79 ± 0.039 cm in group2 DS

7.61 ± 0.026 cm in group 3 normal,7.43 ± 0.087 cm in group3 DS

7.54± 0.056 cm in group 4 normal, 7.32 ± 0.044 cm in group4 DS

7.51± 0.052 cm in group 5 normal, 7.13 ± 0.059 cm in group5 DS

Linear index: The mean value of the linear index was a ratio greater than 2:1, and no significant difference (linear appearance) was observed among different age groups, gender groups and the normal and DS groups.

The mean value of FG is described below.

2.56 ± 0.03 cm in group 1 normal, 2.46 ± 0.08 cm in group1 DS

3.03 ± 0.32 cm in group 2 normal, 2.81 ± 0.03 cm in group2 DS

3.51 ± 0.22 cm in group 3 normal,2.98 ± 0.17 cm in group3 DS

3.84 ± 0.26 cm in group 4 normal,3.22 ± 0.44 cm in group4 DS

4.01 ± 0.09 cm in group 5 normal, 3.03 ± 0.29 cm in group5 DS

The mean value of SO is described below.

5.01 ± 0.19 cm in group 1 normal, 4.76 ± 0.15 cm in group1 DS

5.23 ± 0.22 cm in group 2 normal, 4.90 ± 0.22 cm in group2 DS

5.54 ± 0.32 cm in group 3 normal, 5.08 ± 0.37 cm in group3 DS

5.83 ± 0.29 cm in group 4 normal, 5.22 ± 0.17 cm in group4 DS

6.11 ± 0.12 cm in group 5 normal, 5.02 ± 0.24 cm in group5 DS

The ratio wasapproximately1:1.5.

A positive correlation (r = 0.69) was noted between the distance between the SO, rather than the vertical brain diameter (r = 0.45),

Sex-related differences

In the present study, sexual dimorphism was not observed in most of the CC parameters measured.

The mean of the longitudinal dimensions and measured ratios tended to be smaller in women in the normal population, but for DS individuals, no inter-sex differences were observed in the mean value for any of the measurements.

BAP (males = 16.09± 0.32 cm, females = 15.73 ± 0.24cm, $P < 0.05$)

CC length (males= 7.59 ± 0.21 cm, females= 7.19± 0.16 cm, $P < 0.08$)

FG (males = 3.79 ± 0.15 cm, females = 3.42± 0.18 cm, $P < 0.07$)

SO (males = 5.78 ± 0.15 cm, females = 5.38± 0.33 cm, $P < 0.06$)

No sex difference was found in the splenium diameter.

A decrease of size in the CC diameter was observed in group 5, but it was present only in males. This result is possibly related to atrophic changes in the brain, which are more notable in DS males.

4. Discussions

According to our data, neither sexual dimorphism nor significant differences in the CC dimensions were observed. Nonetheless, the dimensions of the CC were larger in males than in females.

Additionally, a positive correlation was found between the CC and brain longitudinal diameters. In recent years, several studies using MRI scans have been performed to determine the diameters, morphology and sex-related differences of the CC in individuals in various areas of the world (Mourgela et al., 2007; Narr et al.,2002; Paul et al., 2003; Peterson et al., 2001: Prendergast et al., 2015).

Takeda *et al.* (2003) found that the mean longitudinal and vertical diameters of the CC were 69.7 ± 4.15 and 25.9 ± 2.90 mm, respectively, in Japanese males and 69.4 ± 4.33 and 25.8 ± 2.80 mm, respectively, in Japanese females, but with no significant difference between the sexes. They also reported that the length of the CC is in a state of continuous change in different age groups, but the width decreases in some structures, yielding a stretched appearance (Takeda *et al*. 2003).

In contrast, Suganthy *et al.* (2003) concluded from 100 subjects that the mean longitudinal diameter of the CC in males was significantly greater than in females (72.6 ±5.2 mm in Indian males, 70.6 ± 4.0 mm in Indian females). Suganthy also reported that only the length of the CC increased with age, and no change with age occurred in the diameters of other areas of the CC (Suganthy *et al.* 2003).

According to geographic distribution, Gupta *et al.* (2009) found (using MRI) that the mean longitudinal diameter of the CC in the Indian population was 7.57 cm in men and 7.1 cm in women, and the mean width was 3.27 cm in men and 2.59 cm in women. They also reported that the mean width of the splenium of the CC was 1.15 cm in men and 1.17 cm in women. Furthermore, Gupta found that the CC was smaller in the Indian population than in the Caucasian population but larger than in the Japanese population (Gupta *et al.2009*).

In our study, a positive correlation (r = 0.69) was noted between the SO rather than the vertical brain diameter (r = 0.45), but the BAP exhibited a strong positive correlation with the CC length. Thus, the various dimensions of the brain change correlatively with each other.

All the components inside the cranial cavity are in a state of continuous change to preserve its symmetrical appearance; therefore, all diameters of the brain and CC vary with age, resulting in symmetry between the brain and the size of the CC. This relationship is similar to the results of studies by Estruch *et al.* (1997) and Mourgela *et al.,* (2007). Therefore, it might not be correct to attribute differences in hemispheric functions between the sexes to callosal connections.

The DS population exhibits neuropathological complications similar to AD or atrophic changes that begin in the temporal lobe, and CC atrophy may be a marker for AD (Mann, 1988).. Additionally, the DS population exhibits increased ventricular volume with aging (Kesslak et al., 1994). A positive correlation (r = 0.69) was noted between the SO and CC length, which is similar to the findings of a study by Teipel *et al.,* (2003). Additionally, Lawlor reported the same finding obtained by CT scans.

Corresponding Author:
Abdullah G. Alkushi
Department of Anatomy, Faculty of Medicine,
Umm Al-Qura University, Makkah, Saudi Arabia,
POBox- 57039, Postal code: 21955.
Phone: 00966532570960.
E-mail: dr.alkushi@gmail.com

References

1. Bermudez P, Zatorre RJ (2001) Sexual dimorphism in the corpus callosum: methodological considerations in MRI morphometry. Neuroimage 13:1121-1130. doi: 10.1006/nimg.2001.0772.
2. Estruch R, Nicolás JM, Salamero M, Aragón C, Sacanella E, Fernández-Solà J, Urbano-Márquez A (1997) Atrophy of the corpus callosum in chronic alcoholism. JNeurol Sci 146:145 -151. doi: 10.1016/S0022-510X (96)00298-5.
3. Gupta T, Singh B, Kapoor K, Gupta M, Kochhar S (2008) Age and sex related variations in corpus callosal morphology. Nepal Med Coll J 10:215-221.
4. Gupta T, Singh B, Kapoor K, Gupta M, Kochhar S (2009) Normative data of corpus callosal morphology in a north-west Indian population-an autopsy and MRI study. JNMAJNepal Med Assoc 48:46-51.
5. Head, E., Lott, I. T., Wilcock, D. M., & Lemere, C. A. (2016) Aging in Down syndrome and the Development of Alzheimer's disease Neuropathology. Current Alzheimer Research, 13(1), 18–29.
6. Hunter AGW (2001) Management of genetic syndromes. J Forensic Leg Med14:103–129 Ch. 107.

7. Keshavan MS, Diwadkar VA, Debellis M, Dick E, Kotwal R, Rosenberg DR, Sweeney JA, Minshew N, Pettegrew JW. (2002) Development of the corpus callosum in childhood, adolescence and early adulthood. Life Sci70:1909-1922.
8. Kesslak JP, Nagata SF, Lott I, Nalcioglu O (1994) Magnetic resonance imaging analysis of age-related changes in the brains of individuals with down's syndrome. Neurol 44:1039–1045. doi: 10.1212/WNL.44.6.1039.
9. Lacerda AL, Brambilla P, Sassi RB, Nicoletti MA, Mallinger AG, Frank E, Kupfer DJ, Keshavan MS, Soares JC (2005) Anatomical MRI study of corpus callosum in unipolar depression. JPsychiatr Res 39:347-354. doi: 10.1016/j.jpsychires.2004.10.004.
10. Lott IT, Head E (2005) Alzheimer disease and Down syndrome: factors in pathogenesis. Neurobiol Aging 26:383–389. doi: 10.1016/j.neurobiolaging.2004.08.005.
11. Luders E, Narr KL, Zaidel E, Thompson PM, Toga AW (2006) Gender effects on callosal thickness in scaled and unscaled space. Neuroreport 17:1103-1106. doi: 10.1097/01.wnr.0000227987.77304.cc.
12. Mann DM (1988). The pathological association between down syndrome and Alzheimer disease. Mech Ageing Dev43:99– 136. doi: 10.1016/0047-6374(88)90041-3.
13. Menéndez M (2005) Down syndrome, Alzheimer's disease and seizures. Brain Dev 27:246–252. doi: 10.1016/j.braindev.2004.07.008.
14. Mourgela S, Anagnostopoulou S, Sakellaropoulos A, Gouliamos A (2007) An MRI study of sex-and age-related differences in the dimensions of the corpus callosum and brain. Neuroanatomy 6:63-65.
15. Narr KL, Cannon TD, Woods RP, Thompson PM, Kim S, Asunction D, van Erp TG, Poutanen VP, Huttunen M, Lönnqvist J, Standerksjöld-Nordenstam CG, Kaprio J, Mazziotta JC, Toga AW (2002) Genetic contributions to altered callosal morphology in schizophrenia. JNeurosci 22:3720-3729. doi: 20026309.
16. Paul LK, Van Lancker-Sidtis D, Schieffer B, Dietrich R, Brown WS (2003) Communicative deficits in agenesis of the corpus callosum: non literal language and affective prosody. Brain Lang 85:313-324. doi: 10.1016/S0093-934X (03)00062-2.
17. Peterson BS, Feineigle PA, Staib LH, Gore JC (2001) Automated measurement of latent morphological features in the human corpus callosum. Hum Brain Mapp 12:232-245.
18. Plessen KJ, Wentzel-Larsen T, Hugdahl K, Feineigle P, Klein J, Staib LH, Leckman JF, Bansal R, Peterson BS (2004) Altered interhemispheric connectivity in individuals with Tourette's disorder. Am J Psychiatry 161:2028-2037. doi: 10.1176/appi.ajp.161.11.2028. .
19. Prendergast, D., Ardekani, B., Ikuta, T., John, M., Peters, B., DeRosse, P Szeszko, P. R. (2015). Age and Sex Effects on Corpus Callosum Morphology Across the Lifespan. *Human Brain Mapping*, *36*(7), 2691–2702. http://doi.org/10.1002/hbm.22800.
20. Quigley M, Cordes D, Turski P, Moritz C, Haughton V, Seth R, Meyer and ME (2003) Role of the corpus callosum in functional connectivity. AJNR Am J Neuroradiol 24:208-212.
21. Standring S and Crossman AR (2005) (Gray's Anatomy) The Anatomical Basis of Clinical Practice, 2005 39th edition, section 2–chapter22, Elsevier, London, pp 411-414.
22. Suganthy J, Raghuram L, Antonisamy B, Vettivel S, Madhavi C, Koshi R (2003) Gender- and age-related differences in the morphology of the corpus callosum. Clin Anat 16:396-403. doi: 10.1002/ca.10161.
23. Takeda S, Hirashima Y, Ikeda H, Yamamoto H, Sugino M, Endo S (2003) Determination of indices of the corpus callosum associated with normal aging in Japanese individuals. Neuroradiol 45:513-518. doi: 10.1007/s00234-003-1019-8.
24. Tanaka-Arakawa MM, Matsui M, Tanaka C, Uematsu A, Uda S, Miura K, et al. (2015) Developmental Changes in the Corpus Callosum from Infancy to Early Adulthood: A Structural Magnetic Resonance Imaging Study. PLoS ONE 10(3): e0118760. doi:10.1371/journal.pone.0118760.
25. Teipel SJ, Bayer W, Alexander GE, Zebuhr Y, Teichberg D, Kulic L, Schapiro MB, Möller HJ, Rapoport SI, Hampel H (2002) Progression of corpus callosum atrophy in Alzheimer disease. Arch Neurol 59:243-248. doi: 10.1001/archneur.59.2.243.
26. Teipel SJ, Schapiro MB, Alexander GE, Krasuski JS, Horwitz B, Hoehne C, Möller HJ, Rapoport SI, Hampel H (2003) Relation of corpus callosum and hippocampal size to age in nondemented adults with down's syndrome. Am J Psychiatry 160:1870-1878. doi: 10.1176/appi.ajp.160.10.1870.
27. Thompson PM, Dutton RA, Hayashi KM, Lu A, Lee SE, Lee JY, Lopez OL, Aizenstein HJ, Toga AW, Becker JT (2006) 3D mapping of ventricular and corpus callosum abnormalities in

HIV/AIDS. Neuroimage 31:12-23. doi: 10.1016/j.neuroimage.2005.11.043.
28. Tomaiuolo F, Di Paola M, Caravale B, Vicari S, Petrides M, Caltagirone C (2002) Morphology and morphometry of the corpus callosum in Williams's syndrome: a T1-weighted MRI study. Neuroreport 13:2281-2284. doi: 10.1097/01.wnr.0000044222.79663.72.
29. von Plessen K, Lundervold A, Duta N, Heiervang E, Klauschen F, Smievoll AI, Ersland L, Hugdahl K (2002) Less developed corpus callosum in dyslexic subjects-- a structural MRI study. Neuropsychologia 40:1035- 1044. doi: 10.1016/S0028-3932(01)00143-9.
30. Yamauchi H, Fukuyama H, Shio H (2000) Corpus callosum atrophy in patients with leukoaraiosis may indicate global cognitive impairment. Stroke 31:1515-1520. doi: 10.1161/01.STR.31.7.1515.
31. Yasar AS, Monkul ES, Sassi RB, Axelson D, Brambilla P, Nicoletti MA, Hatch JP, Keshavan M, Ryan N, Birmaher B, Soares JC (2006) MRI study of corpus callosum in children and adolescents with bipolar disorder. Psychiatry Res 146:83-85. doi: 10.1016/j.pscychresns.2005.09.004.

1/25/2018