Measurements of the cerebral cortical thickness in healthy Sudanese subjects during third and fourth decades of age

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ABSTRACT

Introduction The cortex is the outer covering of cerebrum that contains the functional areas including motor, sensory, visual, auditory, and speech. Measuring the cortical thickness of the cerebral hemisphere has greater importance because it supports the neuroscientists in their investigations of normal and abnormal changes in the cortical thickness. The aim of the present study was to measure cortical thickness of the cerebral hemisphere, frontal lobe, and frontal lobe gyri in young adult Sudanese in the third and fourth decade and to determine the effect of sex and age on the cortical thickness of cerebral hemisphere and its gyri.

Material and methods The study included 139 healthy Sudanese subjects (80 males and 59 females) ranging between 20-39 years of age; they were assigned into the third and fourth decades. T1-weighted MR brain images with thickness 1mm were obtained. MR images of the subjects were analysed using the automatic segmentation software (BrainSuite). Cerebral cortical thickness (CCT) of the cerebral hemispheres, frontal lobes, and frontal lobe gyri were estimated using the output data of process of the software.

Results The CCT of the cerebral hemispheres (3.810.21±mm) (3.840.16±mm) and frontal lobes (4.26±0.22mm) (4.240.22±mm) during third and fourth decade, respectively was not different between genders ($P>0.05$). Within third decade, there was no gender difference in CCT of frontal lobe gyri, except for the left precentral gyrus. While within fourth decade, the gender difference was reported in the middle frontal, pars opercularis, pars triangularis, precentral and paracentral, and subcallosal gyri ($P<0.05$). CCT of the cerebral hemisphere and frontal lobe did not change from third to fourth decade ($P>0.05$). Changes in CCT from third to fourth decade were noticed in the precentral, paracentral gyri, and pars opercularis.

Conclusion Cortical thickness of the cerebral hemisphere and frontal lobe were not different between genders and was not changed by age; so they are independent values from sex and age. However, gender differences and change by age were reported in some frontal lobe gyri. This data can serve as normative database and reference data for both researchers and clinicians.

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INTRODUCTION

The cerebral cortex composes of grey matter and contains more than 10 billion neurons. The cerebral cortex is thicker over the gyri (4.5mm) than sulci (1.5mm).[1] The thickness of the cortex provides information about the size and number of neuronal cell bodies; synaptic connections, and the myelination of fibers. It was reported that cortical thickness of the frontal lobe may be affected by normal aging and some disease such as Alzheimer, Huntington, and Schizophrenia diseases.[3] Measuring the cortical thickness of the frontal lobe has greater importance, because it

supports the neuroscientists in their investigations of normal and abnormal change in the cortical thickness. Measuring the cortical thickness from magnetic resonance (MR) images can be done by applying the manual and automated methods. The manual methods were used to estimate the cortical thickness from Brain MR images; but are time consuming even by expert anatomist, subjective, and the natural of the cortex, which is highly folded may lead to errors in measurements.[4] Therefore, there is strong demand to perform reliable and accurate automated methods to measure the cortical thickness.

In the present study cortical thicknesses of the cerebral hemisphere, frontal lobe, and frontal lobe gyri were measured from T1 weighted brain MR images by applying automatic segmentation tool called BrainSuite, which is a collection of software tools that automatically calculate cortical thickness of regions of interest from brain MR image.

MATERIAL AND METHODS

The current study includes 139 normal young adult Sudanese subjects ranging between 20-40 years of age. The subjects were assigned into two groups depending on their age decade: third decade (20-29) and fourth decade (30-39) aiming to examine the sex differences with each age decade and structural change between third and fourth decade. The numbers of subjects in the third and fourth decades were 84 and 55, respectively. Matching for age, sex and body mass index (BMI) was performed. Age and BMI of males and females were (28±5.72) and (28±6.00) years; and (23.93±3.6) and (24.89±5.07) kg/cm^2, respectively. The participants were excluded if they are drug abuse, or had head trauma, neurological diseases, psychiatric illnesses, or congenital malformation related to the brain. The study was approved by the Ethical Committee of the National Ribat University.

The sample size was calculated using the following formula, keeping the confidence level equals to 95% and the margin of error equals to 5%.:

$$n = (Z^2)_{(1-\alpha/2)} P (1-P))/d^{(2)}$$

where $(Z^2)_{(1-\alpha/2)}$ = for 95% confidence level = 1.96

P = Anticipated proportion of infant mortality =10% (cite reference).

d = Margin of error = 5%.

n = Sample Size = 140.

(Ref: Sample size determination in health studies version 2.0.21. WHO)

Magnetic resonance (MR) imaging

Structural MR imaging was done in the radiology department, Doctors' Clinic, Khartoum. MR imaging was performed on 1.5 Tesla Philips scanners, Version: 3.2.1. T1-weighted MR brain images obtained using three-dimensional acquisition by Magnetization Prepared Rapid Acquisition (MP-RAGE), acquisition time (5 minutes and 18 seconds), Slice distance was 1.0mm, the field of view was 250 read, 192mm phase, TR=1657ms, TE=2.95ms, bandwidth 180Hz/pixel, flip angle 15°, ECHO spacing=7.5ms, phase resolution=100%, and slice resolution=50%.

MR images analysis

MR images of the subjects were analyzed using automatic segmentation software (BrainSuite 13a), performed on a Toshiba computer Core i3, 2.10 GHz, 6GB. The software analyzed each MR image in two stages: the first stage is cortical surface extraction sequence, which took 30 minutes to run; while the second stage was long and lasted for 2 hours and 15 minute, which was surface and volume registration.

Cortical surface extraction sequence (CSE)

The first step in the CSE was removing of the skull and scalp from MR image. The next steps included classifying the tissue into cerebrospinal fluid (CSF), grey and white matter; and labelling the brain volume into cerebrum, cerebellum, and brainstem. After that the BrainSuite running cortex masked

selection and topology correction: that included extraction of the cerebral cortex and correction of any errors that might occur during that process. The last stages in the cortical surface extraction included the generation of the pial surface and separation of the cortical surface into left and right hemispheres and displayed them with different colour (Figure 1)

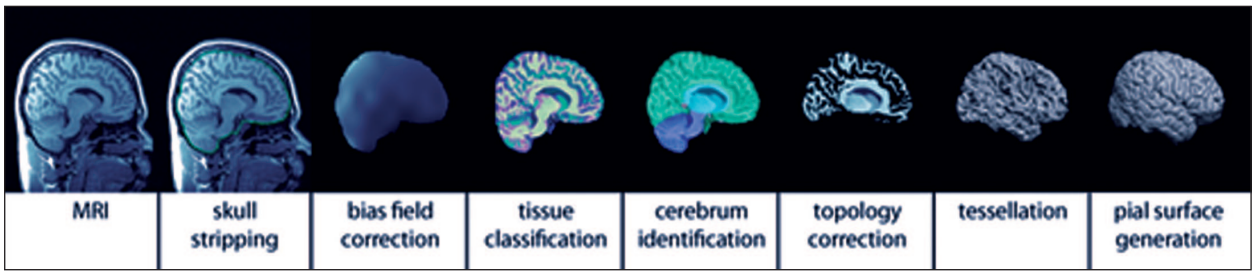

Figure 1. Steps of cortical surface extraction sequence (www.Brainsuite.org)

Surface and volume registration (SVReg)

The SVReg is a programme that registers the results of cortical thickness extraction sequence, which includes the volumes and surfaces to the brain atlas created by expert neuroanatomist. Registering images allows for automatic labelling and analysis of cortical and subcortical structures. (www.Brainsuite.org). Results of SVReg were: labelled inner, pial and mid cortical surfaces of cerebrum; labelled brain volume; and spread sheets of statistics include measurements of the cortical and subcortical structures (Figure 2).

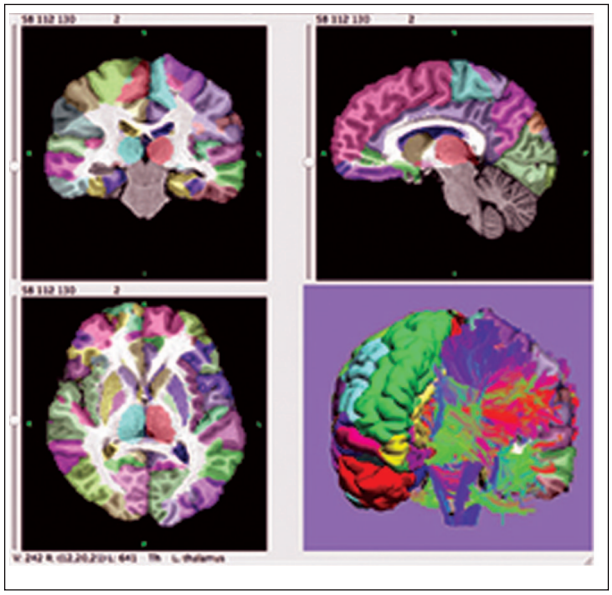

Figure 2. MR image analyzed by BrainSuite (www.Brainsuite.org)

BrainSuite automatically calculate cortical thickness of gyri of the cerebral hemispheres. To calculate cortical thickness of cerebral hemisphere and frontal lobe the following formulae were used in microsoft excel worksheet:

Cortical thickness of the cerebral hemisphere= ∑ cortical thickness of cerebral gyri (1)

Cortical thickness of the frontal lobe= ∑ cortical thickness of frontal lobe (1)

Statistical Analysis

Data were analysed using Statistical Package of Social Science (SPSS) version 21.0; independent sample t.test was performed to compare mean values of cortical thickness between males and females as well as between third and fourth decades. P value equals or less than 0.05 is considered statistically significant.

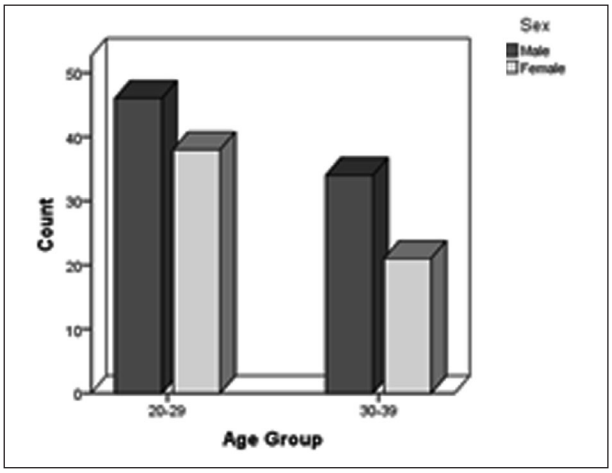

Fig.3: Distributions of subjects according to gender and age decades

RESULTS

Figure 3 shows the number of male and female subjects in the two age group decades.

Sex differences in the cerebral cortical thickness (CCT) depending on Age decade

To determine the gender differences, mean CCT of region of interest was compared between males and females in the third and fourth decades. Within the third decade, there were no differences between genders in the CCT of the hemispheres, frontal lobe, and frontal lobe gyri (P>0.05); with exception of CCT of the total precentral gyri which was larger in females (P<0.05). Within the fourth decade, males had larger CCT in the right middle frontal gyrus, pars opercularis, pars triangularis; in addition to the left and total precentral and paracentral gyri. Conversely, females had larger CCT in the total subcallosal area (P<0.05). There were no differences between genders in the hemispheres, frontal lobe and other frontal lobe gyri (P>0.05). Details of the data of CCT of regions of interest are given in Table.

Change by decade in the cerebral cortical thickness (CCT)

To determine the change by decade, cortical thickness of regions of interest was compared between males during third and fourth decades; and between females during third and fourth decades. Cortical thickness of the hemispheres, frontal lobes, and most of frontal lobe gyri did not change from third to fourth decade in males or females. The change by decades in CCT was demonstrated in the precentral, paracentral and pars opercularis gyri, which was not homogeneous neither in males nor females. In males, from third to fourth decade: CCT of the right precentral and paracentral gyri decreased; conversely, CCT of the left and total precentral; and total paracentral gyri increased. In females, from third to fourth decade: CCT of the left and total precentral; the right and left paracentral gyri and the right pars opercularis decreased. Details of the data of cortical thickness of regions of interest are given in Table.

Table. Cortical thickness of regions of interest

	Cortical Thickness			
	20-29 Years		30-39 Years	
Region of Interest	Males	Females	Males	Females
Rt. Cerebral Hemisphere	3.85±0.14	3.82±0.22	3.81±0.15	3.75±0.17
Lt. Cerebral Hemisphere	3.80±0.18	3.79±0.15	3.84±0.21	3.79±0.12
T. Cerebral Hemisphere	3.80±0.17	3.80±0.15	3.84±0.19	3.80±0.14
Rt. Frontal Lobe	4.28±0.18	4.26±0.29	4.24±0.19	4.19±0.21
Lt. Frontal Lobe	4.27±0.20	4.25±0.26	4.23±0.23	4.30±0.26
T. Frontal Lobe	4.27±0.18	4.26±0.26	4.23±0.20	4.25±0.20
Rt. Superior Frontal	4.70±0.20	4.68±0.26	4.61±0.19	4.66±0.19
Lt. Superior Frontal	4.55±0.27	4.52±0.28	4.56±0.27	4.44±0.22
T. Superior Frontal	4.61±0.25	4.58±0.24	4.63±0.22	4.54±0.16
Rt. Middle Frontal	4.22±0.22	4.20±0.31	4.26±0.21	4.13±0.16C
Lt. Middle Frontal	4.22±0.24	4.22±0.25	4.22±0.22	4.15±0.18
T. Middle Frontal	4.21±0.22	4.21±0.23	4.23±0.21	4.17±0.16
Rt. Pars Opercularis	4.62±0.28	4.52±0.29	4.58±0.37	4.36±0.18BC
Lt. Pars Opercularis	4.48±0.25	4.46±0.24	4.46±0.30	4.41±0.19
T. Pars Opercularis	4.50±0.23	4.49±0.23	4.53±0.24	4.50±0.18
Rt. Pars Triangularis	4.25±0.22	4.15±0.34	4.20±0.27	3.99±0.32C
Lt. Pars Triangularis	4.35±0.25	4.29±0.26	4.33±0.28	4.33±0.23

T. Pars Triangularis	4.26±0.21	4.23±0.22	4.26±0.26	4.23±0.19
Rt. Pars Orbitalis	4.26±0.35	4.20±0.32	4.22±0.30	4.10±0.47
Lt. Pars Orbitalis	4.24±0.40	4.17±0.29	4.35±0.38	4.21±0.40
T. Pars Orbitalis	4.21±0.25	4.20±0.22	4.29±0.28	4.22±0.27
Rt. Precentral	3.52±0.22	3.52±0.23	3.38±0.19A	3.45±0.22
Lt. Precentral	3.26±0.23	3.34±0.23	3.38±0.28A	3.19±0.29BC
T. Precentral	3.34±0.20	3.43±0.18C	3.47±0.23A	3.29±0.22BC
Rt. Paracentral	3.88±0.32	3.95±0.30	3.66±0.24A	3.76±0.29B
Lt. Paracentral	3.66±0.31	3.76±0.30	3.78±0.33	3.61±0.20BC
T. Paracentral	3.71±0.29	3.80±0.25	3.85±0.30A	3.71±0.19C
Rt. Transverse Frontal	4.36±0.66	4.27±0.69	4.43±0.43	4.33±0.43
Lt. Transverse Frontal	4.26±0.56	4.22±0.57	4.23±0.57	4.32±0.46
T. Transverse Frontal	4.32±0.50	4.25±0.53	4.31±0.50	4.32±0.34
Rt. Cingulate	4.08±0.22	4.05±0.24	4.02±0.18	4.03±0.30
Lt. Cingulate	3.99±0.23	4.01±0.23	4.06±0.28	4.02±0.16
T. Cingulate	4.01±0.21	4.02±0.21	4.08±0.23	4.03±0.17
Rt. Subcallosal	3.56±0.89	3.75±0.84	3.42±0.84	3.59±0.82
Lt. Subcallosal	4.47±1.16	4.34±0.99	4.36±0.76	3.95±0.68C
T. Subcallosal	4.03±0.86	3.98±0.68	3.96±0.65	3.72±0.81
Rt. Orbito-Frontal	4.54±0.28	4.51±0.42	4.57±0.31	4.44±0.36
Lt. Orbito-Frontal	4.51±0.36	4.44±0.32	4.58±0.38	4.47±0.31
T. Orbito-Frontal	4.52±0.34	4.47±0.28	4.56±0.32	4.49±0.28

(Mean±SD), A: P ≤0.05 in comparison between males, B: P ≤0.05 in comparison between females C: P ≤0.05 in comparison between sex

DISCUSSION

Sex Differences in the Cerebral Cortical Thickness (CCT) Depend on Age Decade

The present study found that cortical thickness of frontal lobe gyri was ranging from 3.30 to 4.66mm and 3.29 to 4.67mm in males and females, respectively. The lowest cortical thickness of the frontal lobe gyri located in the right superior frontal gyrus and highest cortical thickness of the frontal located in the left precentral gyrus in males and females. The findings of the present study demonstrated that gender differences in CCT depend on age decade; during third decade there were no significant differences in cortical thickness of the hemispheres, frontal lobes, and frontal lobe gyri; with exception of cortical thickness of the total precentral gyrus which were larger in females. During fourth decade gender differences in CT have been reported in the right middle frontal gyrus, pars opercularis, pars triangularis; in addition to the left and total precentral and paracentral gyri; and the total Subcallosal area.

One possible reason for gender differences in CCT includes differences in the rate of maturation and/ or thinning of the cortex at specific age.[2] The findings of the present study confirm this concept; as cortical thickness of precentral and paracentral decrease with age in males but increase with age in females. Other reason for the gender differences in the cortical thickness could be due to differences in the cells numbers, degree of myelination of the white matter and/ or size of the cells.[5]

Change by decade in the cerebral cortical thickness (CCT)

The result of this study found the changes by decades in cortical thickness of the precentral, paracentral

gyri, and pars opercularis. The decrease in CCT from third to fourth decade has been reported in males and females: in males, in the right precentral and paracentral gyri; in females, in the left and total precentral, the right and left paracentral gyri and the right pars opercularis. This decrease in CCT can be explained by the following: shrinkage of neurons,[6] reduction in synaptic density,[7] reduction in spines of dendrites,[8] losing of presynaptic terminals,[9] and alteration of microvasculature.[10] The increase in CCT from third to fourth decade has been reported merely in males in the left and total precentral, and total paracentral gyri. This increase in thickness could be explained by neuronal plasticity induced by learning at an age where functional connectivity maturation is still in progress with the refinement of neuronal connections.[11]

CONCLUSIONS

Cortical thickness of the cerebral hemisphere and frontal lobe were not different between genders in the third and fourth decade; however, gender differences in cortical thickness was reported in some gyri of frontal lobe. Males had larger cortical thickness of the right middle frontal gyrus, pars opercularis, pars triangularis; the left and total precentral and paracentral gyri in the fourth decade and females had larger cortical thickness of the total precentral gyri and subcallosal area with the third and fourth decades, respectively. Cortical thickness of the cerebral hemisphere and frontal lobe showed no change from third and fourth decade, however some gyri of frontal lobe changed with age. From third to fourth decade: cortical thickness of the right precentral and paracentral gyri decreased; but cortical thickness of the left and total precentral; and total paracentral gyri increased in males; cortical thickness of the left and total precentral; the right and left paracentral gyri; and the right pars opercularis decreased in females.

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