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Volumetric Assessment of the Insula in a Normally Functioning Human Brain Using Magnetic Resonance Imaging

Evaluación Volumétrica de la Ínsula en un Cerebro Humano que Funciona Normalmente Utilizando Imágenes de Resonancia Magnética

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SUMMARY: Volumetric assessment of brain structures is an important tool in neuroscience research and clinical practice. The volumetric measurement of normally functioning human brain helps detect age-related changes in some regions, which can be observed at varying degrees. This study aims to estimate the insular volume in the normally functioning human brain in both genders, different age groups, and side variations. A cross-sectional retrospective study was conducted on 42 adult Sudanese participants in Al-Amal Hospital, Sudan, between May to August 2022, using magnetic resonance imaging (MRI) and automatic brain segmentation through a software program (BrainSuite). The statistical difference in total insular volume on both sides of the cerebral hemisphere was small. The insular volume on the right side was greater in males, while the left side showed no difference between both genders. A statistically significant difference between males and females was found ($p > 0.05$), and no statistical difference in different age groups was found according to the one-way ANOVA test ($p>0.05$). Adult Sudanese males showed a larger insular volume than females. MRI can be used to morphometrically assess the insula to detect any pathological variations based on volume changes.

KEY WORDS: Insula; Volumetric; Age group; Sex; DICOM software.

INTRODUCTION

The insula is a complex structure located deep within the cerebral cortex of the brain, between the temporal, parietal, and frontal lobes. This structure is involved in a wide range of functions, including emotion, perception, self-awareness, and social cognition (Craig, 2009; Uddin *et al*., 2017; Turgut *et al*., 2018). The insula is divided into several regions, including the anterior, middle, and posterior insula. The anterior insula is involved in social and emotional processing, while the middle insula is involved in sensory processing. The posterior insula is involved in interception or the perception of internal bodily sensations (Waxman, 2009; Craig, 2009; Uddin *et al*., 2017). The insula is also connected to many other brain regions, including the amygdala, the prefrontal cortex, and the anterior cingulate cortex. These connections play a key role in the insula's function (Craig, 2009; Uddin *et al*., 2017, Lucina Q *et al*., 2017). During fetal brain development, the insula begins to develop at week 13 and is completed at week 18 (Mavridis *et al*., 2011; Öz *et al*., 2021).

Recent research has shed new light on the role of the insula in various conditions, including addiction, depression, and anxiety. For example, studies have shown that the insula is activated in response to drug cues in individuals with substance use disorders, suggesting that it might play a key role in addiction (Naqvi & Bechara, 2010). Other studies have suggested that the insula may be involved in the regulation of mood and emotion, and the dysfunction in this region may contribute to the development of depression and anxiety (Paulus & Stein, 2010).

Studies have used various imaging techniques, including magnetic resonance imaging (MRI), to assess the volume of the insula in normally functioning human brains.

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These studies have reported a wide range of insula volumes, with some studies suggesting that differences in volume may exist between the left and right insula (Paulus & Stein, 2010). The relationship between the insula volume and various cognitive and emotional functions has also been explored. For example, one study found a positive correlation between the insula volume and emotional intelligence (Takeuchi *et al*., 2014). Volumetric assessment of the insula has limitations. For example, differences in image acquisition and processing techniques can affect the accuracy of volume measurements. Additionally, volumetric assessment alone may not provide a complete picture of the insula's structure and function, and other techniques, such as functional imaging, may be needed to fully understand the role of the insula in the human brain.

Despite these limitations, volumetric assessment of the insula remains an important tool in neuroscience research and clinical practice. Further research is needed to better understand the relationship between the insula volume and various cognitive and emotional functions and develop highly accurate and precise methods for volumetric assessment. However, the volumetric measurement of the insula in normally functioning human brains can help identify normal and abnormal patterns and detect early changes. MRI and automatic brain segmentation through a software program (BrainSuite) were performed to estimate the insular volume in both sexes, different age groups, and side variation to establish a baseline data of the normal insular volume in adult Sudanese.

MATERIAL AND METHOD

Study design and population: This is an observational descriptive prospective and retrospective cross-sectional hospital-based study carried out in Al-Amal Hospital, Khartoum State, Sudan, between May 2022 to August 2022. MRI scans were performed on the normally functioning brains of 42 adult Sudanese participants, 18 males and 24 females, with ages ranging from 18 years to 60 years.

Inclusion criteria: Adult Sudanese whose MRI brain scans showed no underlying brain lesion were included. The age of full human brain development is at 18 years to 20 years, and brain atrophic changes occur after the age of 60 (Kalani *et al*., 2009; Johnson *et al*., 2009; Lafta & Imeer, 2019).

Exclusion criteria: Sudanese participants whose MRI brain scans confirm any kind of diseases, lesions, and anomalies were excluded.

Procedure: The Dicom images of the patients were transferred to the Image J software and converted into stack. Blind to clinical data, morphometric measurements were taken using the ImageJ software, where the images were re-sliced, re-oriented, and converted to the Analyze 7.5 image format. The measurements from the images can be stored separately. This software takes valid and reliable measurements of specific structures using a delineation approach. Structural MR images were taken for the participant group using a SIEMENS 1.5 Tesla Magnetom Avanto Vision System scanner. T1-weighted images were obtained using three-dimensional acquisition by magnetization-prepared rapid acquisition. The MR brain images of the subjects were first manually delineated using the Image J program and then automatically segmented through the BrainSuite software. Then, the segmented images were analyzed quantitatively using stereological methods and transferred to the structural brain analysis program. BrainSuite is a collection of image analysis tools designed to process MR images of the human head. BrainSuite provides an automatic sequence to extract cortical surface mesh models from the MR images and tools to register these to a labelled atlas to define anatomical regions of interest and for processing diffusion imaging data. BrainSuite also contains visualization tools for exploring these data and can produce interactive maps of regional connectivity. The images in the Analyze 7.5 image format transferred to the structural brain analysis program underwent the following stages:

- The skull strip stage of the processing is controlled and adjusted manually to guarantee the delineation of the brain tissue.
- The splitting hemispheres, surface, and volume registration stages are done automatically.

Following visual quality control, the volumes of the ROIs were produced by the software, all data were collected on a master sheet designed for this purpose, and volumetric data were calculated in centimeters (cm).

Ethical considerations: Ethical clearance was obtained from the institutional review board at the National University of Sudan, with permission from faculty authorities. Acceptance consent were obtained from the individuals who confirmed the required brain MR images.

Data analysis: The Statistical Package for Social Sciences (SPSS) software, version 23.0 (IBM SPSS Inc., Chicago, IL), was used for data analysis. Both descriptive and inferential statistics involving the Independent T-test, the Mann–Whitney U-Test, the one-way ANOVA (Analysis of Variances) test, The Kruskal–Wallis H-Test, Spearman's rho correlation, and the Pearson correlation test were performed to present the results. A p-value of less than 0.05 is considered statistically significant.

RESULTS

The number of participants in this study was 42, and 24 (57.1 %) were females and 18 (42.9 %) were males. The mean total insula volume on the right side was 4.79 cm3 (±1.51 SD) and 4.84 cm3 (±0.41 SD) on the left side. The mean total insula grey matter volume on the right side was 3.10 cm3 (±1.00 SD) and 3.23 cm3 (±0.38 SD) on the left side. The mean total insula white matter volume on the right side was 1.69 cm3 (±0.63SD) and 1.61 cm3 (±0.38SD) on the left side (Table I). The statistical difference in total volume and grey and white matter on both sides was small.

In the males, the total insula volume on the right side was 6.4839 cm^3 (±0.27498 SD) and 5.0606 cm^3 (±0.48215 SD) on the left side. In the females, the total insula volume on the right was 3.5133 cm^3 (±0.29347 SD) and 4.6783 cm^3 (±0.26009 SD) on the left. On both sides, the total insula volume was greater in the males than in the females. In the males, the total insula volume was greater on the right side, while that in the females was greater on the left side. The volume of the grey and white matter on the right side was greater in the males than in the females, while that on the left side shows no difference between males and females (Table II). A statistically significant difference between males and females was found (p>0.05).

The mean total volume of the left isula in different age groups is as follows: 4.9688 cm^3 (±0.4052 SD) in those below 30 years old, 4.774 cm^3 (±0.36294 SD) in those between 30 and 40 years, and 4.7509 cm^3 (±0.47811 SD) in those above 40 years. No statistical difference in different age groups was found according to the one-way ANOVA test (p>0.05) (Tables III and IV).

Table I. Mean volumes and std. deviations of the gray and white matter of the insula on both sides in 42 adult Sudanese people.

Side	Descriptive Statistics	Minimum	Maximum	Median	Mean	Std. Error of Mean	Std. Devia
Right	Grey matter volume (cm^3)	1.36	4.79	2.735	3.10	0.1538	1.00
	White matter volume (cm^3)	0.96	2.94	1.32	1.69	0.09668	0.63
	Total volume (cm^3)	2.92	6.98	3.875	4.79	0.23368	1.51
Left	Grey matter volume (cm^3)	2.48	4.1	3.215	3.23	0.05854	0.38
	White matter volume (cm^3)	1.12	2.52	1.555	1.61	0.05861	0.38
	Total Insula volume (cm^3)	4.11	5.73	4.815	4.84	0.06381	0.41

Table II. Mean volumes and std. deviations of insula in two sexes using the Independent T-Test.

Independent T-Test							
Side	Variables	Sex	NO	Mean	Std. Deviation	Std. Error Mean	P value
Right	Grey matter Insula volume (cm^3)	Male	18	4.1478	0.4104	0.09673	
		Female	24	2.31	0.36908	0.07534	0.0000001**
	White matter Insula volume (cm^3)	Male	18	2.3361	0.32713	0.07711	
		Female	24	1.2033	0.21661	0.04421	0.0000001**
	Total Insula volume (cm^3)	Male	18	6.4839	0.27498	0.06481	
		Female	24	3.5133	0.29347	0.05991	0.0000001**
Left	Grey matter Insula volume (cm^3)	Male	18	3.4639	0.31092	0.07328	
		Female	24	3.0558	0.33266	0.0679	0.0002**
	White matter Insula volume (cm^3)	Male	18	1.5967	0.45744	0.10782	
		Female	24	1.6225	0.31969	0.06526	0.839*
	Total Insula volume (cm^3)	Male	18	5.0606	0.48215	0.11364	
		Female	24	4.6783	0.26009	0.05309	0.005**

*. P value >0.05 is considered statistically insignificant. **. P value <0.05 is considered statistically significant.

Table III. Mean volumes of insula in different age groups.

One Way ANOVA-Test						
Variables	Age groups	Number	Mean	Std. Deviation	Std. Error	P value
Grey matter Insula volume (cm^3)	Less than 30 years	16	3.605	0.91038	0.22759	
	30-40 years	15	2.7407	0.92504	0.23884	
	More than 40 years	11	2.8464	0.97977	0.29541	0.030**
White matter Insula volume (cm^3)	Less than 30 years	16	1.9619	0.6364	0.1591	
	30-40 years	15	1.5527	0.58124	0.15007	
	More than 40 years	11	1.4773	0.57696	0.17396	0.079*
Total Insula volume (cm^3)	Less than 30 years	16	5.5669	1.45104	0.36276	
	30-40 years	15	4.2933	1.31842	0.34041	
	More than 40 years	11	4.3236	1.49543	0.45089	0.028**
Grey matter Insula volume (cm^3)	Less than 30 years	16	3.3869	0.33336	0.08334	
	30-40 years	15	3.1627	0.36165	0.09338	
	More than 40 years	11	3.0964	0.41774	0.12595	0.100*
White matter Insula volume (cm^3)	Less than 30 years	16	1.5819	0.40864	0.10216	
	30-40 years	15	1.6113	0.41855	0.10807	
	More than 40 years	11	1.6545	0.30379	0.0916	0.892*
Total Insula volume (cm^3)	Less than 30 years	16	4.9688	0.4052	0.1013	
	30-40 years	15	4.774	0.36294	0.09371	
	More than 40 years	11	4.7509	0.47811	0.14416	0.302*

Table IV. Spearman's rho correlation of the insula volume and age.

Spearman's rho correlations							
Variables		grey matter) Right Insula volume (cm^3)	White matter) Right Insula volume (cm3)	(Total) Right Insula volume (cm^3)	Grey matter) Left Insula volume (cm^3)	White matter) Left Insula volume (cm^3)	(Total) Left Insula volume (cm^3)
	Correlation Coefficient	-.318*	-0.292	-.319*	-.363*	0.129	-0.213
	Sig. (2-tailed)	0.04	0.06	0.04	0.018	0.414	0.175
	Number	42	42	42	42	42	42
	Strength	Weak	Weak	Weak	Weak	Weak	Weak
Age groups	Direction	Negative	Negative	Negative	Negative	Positive	Negative

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

Males' brain size and external patterns are larger than those of females, as mentioned in most of the literature. However, knowledge of brain gross anatomy and imaging is of paramount importance to neurosurgeons when dealing with it. Given that the insula is a part of the brain, its biometric measurement shows a difference between the two sexes. Gender has a significant effect on insular volume (P-value of 0.001). Meanwhile, several studies (Virupaksha *et al*., 2012; Nathalie Philippi *et al*., 2020; Öz *et al*., 2021) found no effect from age on both sides of the brain (P-value of 0.015). The result of this study indicates that the total insular volume is greater in males than in females. Moreover, the total insular volume on the right side is greater in males than in females, while that on the left side is greater in females than in males. Differences in the volume of certain brain regions in humans caused by sex is an essential issue. These anatomical differences are largely due to the effects of sex hormones on brain development or the expression of genes on the sex chromosomes, and the behaviors and activities of both sexes play a role in shaping these anatomical differences.

Differences between the left and right hemispheres in healthy individuals have been reported in many previous brain studies. Scalabrini *et al*. (2021) observed that the volume of the left insula is larger than that of the right, which is consistent with the results previously obtained by Durazzo *et al*. (2011). Moreover, the results of this study show that the total insular volume of the left is larger than that of the right, the white matter on the right is greater than that on the left, and the grey matter on the left insula is greater than that on the right. These results indicate the variable asymmetry of the human insula on both sides of the brain. Furthermore, the volume of the white matter on the right side is greater in males than in females, and that on the left is greater in females than in males, with a significant difference (P-value of 0.005). This study also found that the volume of grey matter on both sides is greater in males than in females. The differences in insular regions caused by sex may underlie cognitive functions, such as increased empathy, cooperation, understanding of other individual's mental states, and language, as reported by Rilling *et al*. (2008).

Generally, brain tissues undergo normal development and changes, which can be affected by several factors, such as advanced age, hormones, genetics, stress, and nutrition. The studies of Peters (2006) and Scahill *et al*. (2003) showed an inverse relationship between the insular volume and age. They stated that the insula volume declines with age at a rate of approximately 5 % per decade after the age of 40. This study found statistical significant negative correlations between age and the insular volume (P-value of 0.319). Most of the data suggests that atrophy of the insular cortex may be caused by the early stage of Alzheimer's disease (Foundas *et al*., 1997).

The asymmetry of the insular volume on both sides was debated upon in some reports. Virupaksha *et al*. (2012) found the reversal of the asymmetry in the right-left insula in male patients; the left insular volume is larger than the right volume in normal male individuals. Others show left toward asymmetry, suggesting a subtle but significant positive correlation between the extent of hemispheric language dominance and the insula volume asymmetry (Faillenot *et al*., 2017). The results of this study show asymmetry of the insular volume in the right and left sides, that is, the volume in the left side is larger than that in the right side. This finding is consistent with the results of Ackermann & Riecker (2004), that is, the majority of humans display asymmetry in insular volume, indicating that a large insula predicted functional lateralization to the same hemispheric side for most of the subjects.

CONCLUSION

The results of this study provide a reference of ranges of insular volumes and lateralization indices for adult Sudanese people and show a significant difference in the male and female insular volumes and architectures. Males show a larger insular volume than females, larger white matter on the right and grey matter on the left side.

Therefore, we recommend further measurements of other brain regions to detect associated changes with the insular volume and manual analysis for comparison with the automatic one to calculate the annual rate of insular shrinking.

ELGHAZALY, E. A.; RAHMA, A. M. & ELFAKI, A. A. Evaluación volumétrica de la ínsula en un cerebro humano que funciona normalmente utilizando imágenes de resonancia magnética. *Int. J. Morphol., 41(4)*:1171-1176, 2023.

RESUMEN: La evaluación volumétrica de las estructuras cerebrales es una herramienta importante en la investigación y la práctica clínica de la neurociencia. La medición volumétrica del cerebro humano, que funciona normalmente, ayuda a detectar cambios relacionados con la edad en algunas regiones, las cuales se pueden observar en diversos grados. Este estudio tuvo como objetivo estimar el volumen insular en el cerebro humano que funciona normalmente, en ambos sexos, de diferentes grupos de edad y sus variaciones laterales. Se realizó un estudio retrospectivo transversal en 42 participantes sudaneses adultos en el Hospital Al-Amal, Sudán, entre mayo y agosto de 2022, utilizando imágenes de resonancia magnética y segmentación automática del cerebro a través de un software (BrainSuite). Fue pequeña la diferencia estadística en el volumen insular total, en los hemisferios cerebrales. El volumen insular del lado derecho fue mayor en los hombres, mientras que el lado izquierdo no mostró diferencia entre ambos sexos. Se encontró una diferencia estadísticamente significativa entre hombres y mujeres ($p > 0,05$), y no se encontró diferencia estadística en los diferentes grupos de edad, según la prueba de ANOVA de una vía ($p> 0,05$). Los hombres sudaneses adultos mostraron un mayor volumen insular que las mujeres. La resonancia magnética se puede utilizar para evaluar morfométricamente la ínsula y para detectar cualquier variación patológica basada en cambios de volumen.

PALABRAS CLAVE: Ínsula; Volumétrico; Grupo de edad; Sexo; Programa.

REFERENCES

Ackermann, H. & Riecker, A. The contribution of the insula to motor aspects of speech production: a review and a hypothesis. *Brain Lang., 89(2)*:320-8, 2004.

Craig, A. D. How do you feel – now? The anterior insula and human awareness. *Nat. Rev. Neurosci., 10(1)*:59-70, 2009.

Durazzo, T. C.; Tosun, D.; Buckley, S.; Gazdzinski, S.; Mon, A.; Fryer, S. L. & Meyerhoff, D. J. Cortical thickness, surface area, and volume of the brain reward system in alcohol dependence: relationships to relapse and extended abstinence. *Alcohol Clin. Exp. Res., 35(6)*:1187-200, 2011.

Faillenot, I.; Heckemann, R. A.; Frot, M. & Hammers, A. Macroanatomy and 3D probabilistic atlas of the human insula. *Neuroimage, 150*:88-98, 2017.

Foundas, A. L.; Leonard, C. M.; Mahoney, S. M.; Agee, O. F. & Heilman, K. M. Atrophy of the hippocampus, parietal cortex, and insula in Alzheimer's disease: a volumetric magnetic resonance imaging study. *Neuropsychiatry Neuropsychol. Behav. Neurol., 10(2)*:81-9, 1997.

Johnson, S. B.; Blum, R. W. & Giedd, J. N. Adolescent maturity and the brain: the promise and pitfalls of neuroscience research in adolescent health policy. *J. Adolesc. Health, 45(3)*:216-21, 2009.

Kalani, M. Y.; Kalani, M. A.; Gwinn, R.; Keogh, B. & Tse, V. C. Embryological development of the human insula and its implications for the spread and resection of insular gliomas. *Neurosurg. Focus, 27(2)*:E2, 2009.

Lafta, G. A. & Imeer, A. T. The study on incidence of brain atrophy in population with different educational levels. *Biochem. Cell. Arch., 19(2)*:3213-6, 2019.

Mavridis, I.; Boviatsis, E. & Anagnostopoulou, S. Exploring the neurosurgical anatomy of the human insula: a combined and comparative anatomic-radiologic study. *Surg. Radiol. Anat., 33(4)*:319-28, 2011.

Naqvi, N. H. & Bechara, A. The insula and drug addiction: an interoceptive view of pleasure, urges, and decision-making. *Brain Struct. Funct., 214(5-6)*:435-50, 2010.

Öz, F.; Acer, N.; Katayıfçı, N.; Aytaç, G.; Karaali, K. & Sindel, M. The role of lateralisation and sex on insular cortex: 3D volumetric analysis. *Turk. J. Med. Sci., 51(3)*:1240-8, 2021.

Paulus, M. P. & Stein, M. B. Interoception in anxiety and depression. *Brain Struct. Funct., 214(5-6)*:451-63, 2010.

Peters, R. Ageing and the brain. *Postgrad. Med. J., 82(964)*:84-8, 2006.

Philippi, N.; Noblet, V.; Hamdaoui, M.; Soulier, D.; Botzung, A.; Ehrhard, E.; Cretin, B.; Blanc, F. & AlphaLewyMA study group. The insula, a grey matter of tastes: a volumetric MRI study in dementia with Lewy bodies. *Alzheimers Res. Ther., 12(1)*:79, 2020.

Rilling, J. K. Neuroscientific approaches and applications within anthropology. *Am. J. Phys. Anthropol., Suppl. 47*:2-32, 2008.

Scahill, R. I.; Frost, C.; Jenkins, R.; Whitwell, J. L.; Rossor, M. N. & Fox, N. C. A longitudinal study of brain volume changes in normal aging using serial registered magnetic resonance imaging. *Arch. Neurol., 60(7)*:989-94, 2003.

Scalabrini, A.; Wolman, A. & Northoff, G. The self and its right insula-differential topography and dynamic of right vs. left insula. *Brain Sci., 11(10)*:1312, 2021.

Takeuchi, H.; Taki, Y.; Nouchi, R.; Hashizume, H.; Sassa, Y.; Sekiguchi, A.; Kotozaki, Y.; Nakagawa, S.; Nagase, T.; Miyauchi, C. M.; *et al*. Anatomical correlates of quality of life: evidence from voxel-based morphometry. *Hum. Brain Mapp., 35(5)*:1834-46, 2014.

Turgut, M.; Yurttas, C. & Tubbs, R. S. *Island of Reil (Insula) in the Human Brain. Anatomical, Functional, Clinical and Surgical Aspects*. Amsterdam, Springer Cham, 2018. pp.292, 294-303.

Uddin, L. Q.; Nomi, J. S.; Hébert-Seropian, B.; Ghaziri, J. & Boucher, O. Structure and function of the human insula. *J. Clin. Neurophysiol., 34(4)*:300-6, 2017.

Virupaksha, H. S.; Kalmady, S. V.; Shivakumar, V.; Arasappa, R.; Venkatasubramanian, G. & Gangadhar, B. N. Volume and asymmetry abnormalities of insula in antipsychotic-naive schizophrenia: a 3-tesla magnetic resonance imaging study. *Indian J. Psychol. Med., 34(2)*:133-9, 2012.

Waxman, S. G. *Clinical Neuroanatomy*. 26th ed. New York, McGraw-Hill Medical, 2009. pp.79-92.

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